HAVE YOU JOINED CONGRESS (SYDNEY, AUGUST, 1955)?

PUBLISHED WEEKLY

PRICE TWO SHILLINGS AND SIXPENCE

UNIVERSITY OF MICHIGAN
JUL 15 1955
MEDICAL

THE MEDICAL JOURNAL OF AUSTRALIA

VOL. I.—42ND YEAR SYDNEY, SATURDAY, MAY 7, 1955 No. 19

COMMONWEALTH OF AUSTRALIA

Department of Health

INSULIN PREPARATIONS

INSULIN is quick-acting, and may be obtained as follows:—

5 c.c. bottles containing 10 units per c.c.
10 c.c. bottles containing 20 units per c.c.
10 c.c. bottles containing 40 units per c.c.
10 c.c. bottles containing 80 units per c.c.

PROTAMINE ZINC INSULIN is long-acting, and is available in the following strengths:—

10 c.c. bottles containing 40 units per c.c.
10 c.c. bottles containing 80 units per c.c.

NEUTRAL PROTAMINE INSULIN (N.P.H.) contains less protamine and zinc than does Protamine Zinc Insulin, and has an action intermediate between that of Insulin and Protamine Zinc Insulin. This product is available as follows:—

10 c.c. bottles containing 40 units per c.c.
10 c.c. bottles containing 80 units per c.c.

Supplies may be obtained from all offices of the Commonwealth Department of Health in Australia.

COMMONWEALTH SERUM LABORATORIES
PARKVILLE, N.2, VICTORIA, AUSTRALIA

ALWAYS SPECIFY C.S.L. PRODUCTS WHEN PRESCRIBING

SL.81

Registered at the G.P.O., Sydney, for transmission by post as a newspaper.

NOW AVAILABLE!

ANDREW'S CORTISONE ACETATE

***ORAL:** 5 mg. tablets: bottles of 50.
25 mg. tablets: bottles of 20 and 40.

***INJECTABLE:** Saline Suspension for intramuscular use.
25 mg. per c.c.: vials of 20 c.c.

OPHTHALMIC: 1.5% Ointment: tubes of ⅛ oz.

Andrew's "CORTOMYCIN" Ointment:
1.5% Cortisone Acetate combined with
0.5% Neomycin Sulfate.

OPHTHALMIC: tubes of ⅛ oz.

made in Australia

CORTISONE and HYDROCORTISONE preparations

ANDREW'S HYDROCORTISONE ACETATE

ORAL: 10 mg. tablets: bottles of 25.
20 mg. tablets: bottles of 25.

INJECTABLE: Saline Suspension for intra-articular use.
25 mg. per c.c.: vials of 5 c.c.

TOPICAL: 1% and 2.5% ointment: tubes of ½ oz.

DENTAL: 2.5% ointment: tubes of ½ oz.

OPHTHALMIC: 1% ointment: tubes of ⅛ oz.

Andrew's "HYDROCORTOMYCIN" Ointment:
1% Hydrocortisone Acetate combined with
0.5% Neomycin Sulfate.

TOPICAL: tubes of ½ oz.

OPHTHALMIC: tubes of ⅛ oz.

Further literature and information on request from the manufacturers

ANDREW'S LABORATORIES
15 HAMILTON STREET, SYDNEY

MANUFACTURERS OF DRUGS AND FINE CHEMICALS

**Prescribable according to Second Schedule (Restricted Drugs) of the P.B.A.*

AL.44A.FP

THE MEDICAL JOURNAL OF AUSTRALIA

VOL. I.—42ND YEAR SYDNEY, SATURDAY, MAY 7, 1955 No. 19

Table of Contents.

[The Whole of the Literary Matter in THE MEDICAL JOURNAL OF AUSTRALIA is Copyright.]

ORIGINAL ARTICLES— Page.

Progress in Epidemiology and Control of Poliomyelitis, by D. W. Johnson 669
Studies in Portal Hypertension: Estimated Portal Pressure and Hepatic Blood Flow in Patients with Cirrhosis of the Liver and Other Disorders, by A. W. T. Edwards 671
Rupture of the Spleen, by J. L. Connell, M.S., F.R.C.S., F.R.A.C.S. 676

REPORTS OF CASES—

Cardio-Œsophageal Intussusception and Operative Cure, by Kenneth W. Starr 683
Aspiration Biopsy of the Kidney in the Appraisal of Unilateral Renal Disease with Hypertension: Report of a Case, by Brian L. Marks 684

REVIEWS—

Illustrated Handbook of Child Care 687
The Care of Children 687
Text-Book of Ophthalmology 687
Ancient Therapeutic Arts 688

NOTES ON BOOKS, CURRENT JOURNALS AND NEW APPLIANCES—

The "Stellar Filter" 688

BOOKS RECEIVED 688

LEADING ARTICLES—

The Evaluation of Remedies 689

CURRENT COMMENT—

Nutritional Factors in Iron-Deficiency Anæmia 690
Acute Poisoning with Iron Salts 691
Psychogenic Rheumatism 692
The Prophylaxis of Cardiac Infarction 692
Atomic Radiation as an Occupational Hazard 692
Intravenous Caffeine Therapy for Headaches 693
Cigarettes, Whisky and Coronary Disease 693

ABSTRACTS FROM MEDICAL LITERATURE—

Radiology 694
Physical Therapy 695
Surgery 695

ON THE PERIPHERY—

Medicine's Unheeded Handmaiden 696

OUT OF THE PAST 698

MEDICAL SOCIETIES— Page.

The Medical Sciences Club of South Australia .. 698
Medical Defence Society of Queensland 699

CORRESPONDENCE—

Young Doctors and Specialization 699
Pyrimethamine in Emergency Cases of Malaria .. 700
Mortgaging the Future 700
The Use of PAS in Rheumatoid Arthritis 700
James Thomas Rudall, F.R.C.S. (1828-1907): Life and Journal for the Year 1858 701

OBITUARY—

Denis Adrian Pritchard 701
Francis John Meagher 702
John Hardie 702

NAVAL, MILITARY AND AIR FORCE—

Appointments 702

THE ROYAL AUSTRALASIAN COLLEGE OF PHYSICIANS—

Research Fund 703

MEDICAL PRIZES—

David Anderson-Berry Prize (1956) 703

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA 703

PUBLIC HEALTH—

Dangerous Drugs Act, 1934, of South Australia .. 703

CONGRESSES—

Third World Congress of Jewish Physicians 704

AUSTRALIAN MEDICAL BOARD PROCEEDINGS—

Queensland 704

NOMINATIONS AND ELECTIONS 704

MEDICAL APPOINTMENTS 704

DEATHS 704

DIARY FOR THE MONTH 704

MEDICAL APPOINTMENTS: IMPORTANT NOTICE .. 704

EDITORIAL NOTICES 704

PROGRESS IN EPIDEMIOLOGY AND CONTROL OF POLIOMYELITIS.[1]

By D. W. JOHNSON,

Department of Health and Home Affairs, Brisbane.

UNDER the auspices of the World Health Organization, I recently visited the United States, Canada and Europe, and returned to Australia in November, 1954. As a public health administrator, I was particularly interested in learning of new developments in the control of poliomyelitis and of hearing the views of prominent virologists and epidemiologists about the spread of virus from person to person. Tonight, very briefly, I will outline what I consider to be important advances in our knowledge of this disease.

SPREAD OUTSIDE THE BODY.

Despite much research, there is still no definite evidence as to the relative frequency of spread of poliomyelitis virus from the mouth and from the fæces. There is no doubt that both methods of spread can occur. A person incubating the disease has virus in the pharynx for a few days before the onset until a few days after, and presumably can spread the virus by droplet infection during that period. In this way, household contacts would quickly become infected. The phase of alimentary multiplication is much more prolonged—occasionally as long as four months—and during that time virus is discharged intermittently or continuously in the fæces. Faulty personal hygiene in an intestinal excretor can obviously permit widespread dissemination of the virus to food, to water and to objects of common contact. Last year in Sabin's laboratory, a monkey harbouring type II and type III virus was infected with type I virus, presumably from a monkey in the cage above who had a type I infection. Apparently infection was spread by fæcal or dust particles containing type I virus.

Studies have been made to trace the spread of infection in households. Dr. John Paul, of Yale University, has studied household infections, and one particular household in south-west Connecticut illustrates the speed of spread. This household consisted of father (aged thirty-seven years), mother (aged thirty-four years), and four children (aged ten, seven, four and one and a half years). The child aged four years developed a mild illness. Four days later the youngest child became off colour and excreted virus. A day later the child aged ten years developed fever with subsequent paralysis and excretion of virus. A few days later the father developed a sore throat and excreted virus. Of the family of six persons, four became infected within a week. It is now generally believed that multiple clinical cases occur in 3% to 5% of infected households (Report of Committee for Evaluation of Gamma Globulin, 1954), but the interval between the first and second cases is within five days in 60% of cases and within

[1] Read at a meeting of the Queensland Branch of the British Medical Association on March 4, 1955.

twelve days in 90%. Paffenbarger and his colleagues (1954), after investigating outbreaks in Minnesota and Texas, found that previous contact with infected persons was reported by 25% of poliomyelitis patients, and that the proportion of contacts attacked varied directly with the intimacy and duration of contact. Bodian and Paffenbarger (1954) have shown that most, if not all, persons in a household where a clinical case occurs become fæcal carriers shortly after diagnosis of the index case, and that the person who introduces the virus into a household is not necessarily the person who develops clinical disease. In fact, young children frequently introduce the virus into a household. These workers took serum specimens from 137 child contacts within a few days of onset of the index case in the households studied. Five child contacts had viræmia, of whom four experienced symptoms of abortive poliomyelitis, but one child remained quite well. Thirty-three children developed a tenfold rise in antibody titre within a month, but remained well; 81 children already had high antibody levels and therefore were presumably immune; while only 18 developed no antibodies at all in the interval between the tests and therefore presumably were not infected. Two-thirds of all contacts from whom blood was taken showed an antibody rise within five days of the onset of the index case. All these facts indicate that poliomyelitis virus in households has about the same infectivity as chicken-pox.

Where does virus go between seasons? Sabin attempted to find out by taking rectal swabs of 1566 children in Cincinnati orphanages during winter. He was able to grow poliomyelitis virus from only five patients, and not one of these carried the common type I. It appears that the virus lives on in a few intestinal carriers during winter, but for some reason yet unknown, rapid dissemination and multiplication occur as the external temperature rises. By whatever route it is introduced to the human body, poliomyelitis virus behaves in a characteristic way. Virus can be recovered from the oro-pharynx for a few days before the onset of symptoms and for a few days after. Although too few studies have been carried out, there is little doubt that viræmia occurs in persons who have not a protective amount of antibody. Viræmia occurs before the onset of symptoms such as malaise, sore throat and fever. Virus probably enters the cord and medulla directly from the blood rather than along peripheral nerves (Bodian, 1954*a*). Different strains appear to vary in invasive capacity—for example, the Mahoney strain causes paralysis more often than the Saukett or YSK strains. Viræmia can occur in monkeys as early as the second day after inoculation. Virus spreads to the intestinal tract, and in most patients spread to the blood can occur from this site.

Provoking Effect of Injections or Trauma.

The role of prophylactic inoculations, particularly of pertussis vaccine, in causing localization of paralysis to the injected limb was first demonstrated by McCloskey (1950) and has since been abundantly confirmed.

Recent work by Bodian (1954*b*) with cynomolgus monkeys indicates that even non-irritant material (such as normal saline) injected into a limb can predispose that limb to paralysis; but the more irritant the material injected, the more pronounced is the provoking action. He thinks that the provoking effect can best be explained by a reflex effect on vascular penetrability in the appropriate segment of the spinal cord, though on this basis it is difficult to understand the effect of tonsillectomy performed years before in predisposing to bulbar poliomyelitis.

Immunization Against Poliomyelitis.

Passive Immunization.

In 1953, Hammon and his co-workers analysed the findings of a controlled field study of 55,000 children, presumably exposed to poliomyelitis. Approximately half the children were given γ globulin (0·14 millilitre per pound of body weight) and half received an injection of gelatin. They were followed up for fourteen weeks of a poliomyelitis season. Results were statistically significant. Cases occurring during the first week following γ globulin administration were modified in severity. During the next period of four weeks, a high but not complete degree of protection was demonstrated, whilst during the sixth and seventh weeks after injection there was waning protection.

As a result of these findings, the United States Public Health Service sponsored a national programme for evaluation of γ globulin in the summer of 1953. A total of 235,000 children received γ globulin. Unfortunately there were no controls. In the great majority of household contacts, γ globulin was given within five days of the onset of illness in the index cases, though Hammon, in a minority report, was of the opinion that the γ globulin was given far too late, in most of the epidemics studied, to have much or any effect. The committee evaluating the trial was unable to demonstrate that γ globulin was of value in community prophylaxis.

Meanwhile, Hammon and his colleagues (1954) had given further attention to Hammon's original field study. There were 94 patients with poliomyelitis in this study who developed the disease within nine weeks of inoculation. Of these, 68 had received gelatin and 26 γ globulin. By isolation of virus from fæces, and by virus neutralization and complement fixation, it was possible to confirm the diagnosis of poliomyelitis in 73 patients. The remaining 21 patients gave evidence either of infection with other viruses or no evidence of infection with any virus. Of the 73 subjects, 57 had received gelatin and 16 γ globulin. When poliomyelitis ensued in children given γ globulin, and when the onset of the disease had occurred not less than three days or more than eight weeks after the injection, 75% of children appeared to have been protected against paralysis. These results were significant.

When these findings are summarized, it appears that γ globulin is of value in the prophylaxis of paralytic poliomyelitis, though its proper place is still uncertain. Bodian (1954*b*) states that γ globulin is no longer effective in monkeys when given as late as three days after feeding them with virus, and, in view of the speed of spread, it is obviously desirable to give it to household contacts as soon as possible after diagnosis of the index case. No one can yet answer the question as to how long after exposure γ globulin can be given with benefit to contacts. However, it seems to have a noticeable effect early in the incubation period. At present, it is the recommended practice in Australia that, if γ globulin is given to contacts, it should be given within four days of the onset of the index case in a household.

Active Immunization.

Salk Vaccine.

The idea of a poliomyelitis vaccine is not new. Twenty years ago, Kolmer's and Brodie's vaccines were used, but their use in human beings was discontinued after a warning that paralytic poliomyelitis, frequently limited to the inoculated limbs, had been observed. These accidents may have been due to imperfect attenuation of the virus, or they may have been provoked by the injection itself.

Poliomyelitis vaccines were not developed further until 1949 when Enders, Weller and Robbins showed that poliomyelitis virus could be grown in human and monkey tissues of non-nervous origin—an achievement of fundamental importance, because now it was possible to prepare vaccines free of nervous tissue, which is a dangerous inoculum. In 1953 Salk and his colleagues, after extensive experience with formalinized influenza vaccines, published preliminary results of experiments on human beings using poliomyelitis vaccines inactivated with formaldehyde. They showed that viruses of the three immunological types grown in monkey kidney or testicular tissue, when treated with formaldehyde, induced antibody response to all three types on inoculation, and that the antibodies so induced persisted for at least four months. The preparation used did not cause lesions in monkeys.

Later in 1953, Salk and his colleagues carried out experiments which indicated that the proper use of inactivated (formalinized) vaccine would induce the formation of antibodies in non-immune persons, antibody levels in some

persons being raised to the levels found in persons who had had natural infections. In persons who had already developed antibodies against one or more types of virus, injection of the vaccine resulted in very high antibody levels. Further, a booster-like effect was observed when a single injection of vaccine was given to persons who had received three doses of vaccine seven months previously.

On the advice of a committee of experts, the National Foundation for Infantile Paralysis carried out nation-wide trials with the Salk vaccine during the period March to June, 1954. In addition, some 50,000 children in Canada and 20,000 children in Finland received the vaccine. A total of approximately 650,000 children, aged five to nine years, took part in the trials, of whom 200,000 children received a placebo which resembled poliomyelitis vaccine in appearance. Neither the children nor the persons giving the injections knew which was placebo and which was vaccine.

This was a major undertaking, but assessment of the results of the trial is an even more formidable task. The results of serum neutralization tests of inoculated children, together with results of virus culture and serological tests on inoculated children who develop poliomyelitis, are all being forwarded to a committee under Dr. Thomas Francis of the University of Michigan, Ann Arbor. The report of the evaluation committee will be available some time this year, but not earlier than April. Needless to say, it is awaited with considerable interest.

An ideal poliomyelitis vaccine should have the following qualities: (i) It should be safe. (ii) It should protect persons against paralytic disease, in spite of repeated exposure to the virus, for at least one poliomyelitis season. (iii) Reinforcing or booster doses should not be required more frequently than every two or three years. (iv) It should not produce reactions of sensitization, so that repeated doses may be given if required. (v) It should retain its potency when stored.

How far does the Salk vaccine meet these criteria? Before being issued for trial, each batch of the vaccine was tested by tissue culture and by animal inoculation. Because the vaccine is propagated in monkey kidney tissues, it was felt that there was a possibility of damage to human kidneys. So far, there are no indications that this occurs. Another possibility is that sensitization to the Rh factor could occur in children receiving the vaccine. This aspect is still under study. There appears to have been a remarkable freedom from side effects in inoculated children, and it can be concluded that the vaccine is safe.

The second and third criteria cannot yet be answered. All that is known is that persons receiving the vaccine develop antibodies to the three viruses, and that a recall or booster dose causes a further rise in antibodies. Whether the antibody level is sufficient to protect the majority of inoculated children from paralytic disease will be known only later this year. Almost as important is the duration of protective action. Protection by vaccine during childhood might well lead to an increased incidence of the disease in older age groups, since the antibody levels fall with increasing age. A vaccine which requires a reinforcing dose every year is hardly practical.

Nevertheless, it is clear that the development of the Salk vaccine and its subsequent clinical trials represent a major advance in the control of poliomyelitis.

Live Vaccine.

Most virologists believe that the best protection against poliomyelitis is a vaccine of living virus. Such vaccines are a possibility. Dr. Sabin has developed a variant of type II virus which is not neurotropic and which produces high antibody levels in volunteers to whom it is fed, and he is now working with the other types variants. Dr. Cox and his co-workers at Lederle Laboratories have developed avirulent type I and type II viruses, whilst Dr. Schaeffer and Dr. Li, at Montgomery, Alabama, have isolated a non-neurotropic type I virus.

All these will be available for trial should the report on the Salk vaccine be unfavourable. However, it is clear that there will be no widespread trials of a live vaccine if the inactivated vaccine is successful.

SUMMARY.

Poliomyelitis virus spreads quickly in households into which it is introduced, and most members of a household become infected with virus within a week, though there may be only one member who develops clinical evidence of the disease.

Different strains of poliomyelitis vary in their capacity to produce paralytic disease.

The well-known provocative effect of injections in predisposing to paralysis in the injected limb now appears to be due to direct invasion by virus of those segments of the spinal cord supplying the injected limb.

Gamma globulin is of value in preventing paralytic disease in household contacts, but it must be given to contacts as soon as possible after diagnosis of the index case.

The development of the Salk formalinized vaccine represents an important advance in the prophylaxis of poliomyelitis. The vaccine is safe, but the degree and duration of protection conferred by the Salk vaccine will not be known until the report of the evaluation committee is released later this year.

Should the Salk vaccine prove ineffective, there is every prospect of early development of vaccines containing living but attenuated virus.

BIBLIOGRAPHY.

BODIAN, D. (1954*a*), "Viræmia in Experimental Poliomyelitis", *Am. J. Hyg.*, 60: 339.

BODIAN, D. (1954*b*), "Viræmia in Experimental Poliomyelitis", *Am. J. Hyg.*, 60: 358.

BODIAN, D., and PAFFENBARGER, R. S., JUNIOR (1954), "Poliomyelitis Infection in Households. Frequency of Viræmia and Specific Antibody Response", *Am. J. Hyg.*, 60: 83.

ENDERS, J. F., WELLER, T. H., and ROBBINS, F. C. (1949), Cultivation of the Lansing Strain of Poliomyelitis Virus in Cultures of Various Human Embryonic Tissues", *Science*, 109: 85.

HAMMON, W. McD., CORIELL, L. L., LUDWIG, E. H., MCALLISTER, R. M., GREENE, A. E., SATHER, G. E., and WEHRLE, P. F. (1954), "Evaluation of Red Cross Gamma Globulin as a Prophylactic Agent for Poliomyelitis", *J.A.M.A.*, 156: 21.

HAMMON, W. McD., CORIELL, L. L., WEHRLE, P. F., and STOKES, J., JUNIOR (1953), "Evaluation of Red Cross Gamma Globulin as a Prophylactic Agent for Poliomyelitis", *J.A.M.A.*, 151: 1272.

MCCLOSKEY, B. P. (1950), "The Relation of Prophylactic Inoculations to the Onset of Poliomyelitis", *Lancet*, 1: 659.

PAFFENBARGER, R. S., JUNIOR, WILSON, V. O., BODIAN, D., and WATT, J. (1954), "The Spread of Poliomyelitis; An Analysis of Contact during Epidemic Periods", *Am. J. Hyg.*, 60: 63.

REPORT OF COMMITTEE FOR EVALUATION OF GAMMA GLOBULIN (1954), "Evaluation of Gamma Globulin in Prophylaxis of Poliomyelitis", *J.A.M.A.*, 154: 1086.

SALK, J. E., with the collaboration of BAZELEY, P. L., BENNETT, B. L., KRESCH, U., LEWIS, L. J., WARD, E. N., and YOUNGER, J. S. (1954), "Studies in Human Subjects on Active Immunization Against Poliomyelitis", *Am. J. Pub. Health*, 44: 994.

SALK, J. E., with the collaboration of BENNETT, B. L., LEWIS, L. J., WARD, E. N., and YOUNGER, J. S. (1953), "Studies in Human Subjects on Active Immunization Against Poliomyelitis", *J.A.M.A.*, 151: 1081.

STUDIES IN PORTAL HYPERTENSION: ESTIMATED PORTAL PRESSURE AND HEPATIC BLOOD FLOW IN PATIENTS WITH CIRRHOSIS OF THE LIVER AND OTHER DISORDERS.

By A. W. T. EDWARDS,[1]

Clinical Research Unit,[2] Royal Prince Alfred Hospital, Sydney.

THE estimation of portal pressure in patients with liver disease is desirable in the assessment of present status and progress. Serial measurements of a patient's portal pressure made over months or years, in conjunction with liver function tests and the usual methods for detection of

[1] Medical Board Fellow in Medicine.

[2] Supported in part by a grant from the National Health and Medical Research Council.

œsophago-gastric varices, will give a far more comprehensive picture of his progress than criteria based largely on clinical signs and the occurrence of bleeding. This is of great importance to the patient as surgical means are now available for lowering portal pressure and postponing or preventing the lethal complication of hæmorrhage.

Hepatic blood flow is also of interest in studying the progress of liver disease and appears to assume importance in relation to the pathogenesis of hepatic coma, particularly as a complication of shunting operations which divert all or part of the portal blood from the liver. However, values for hepatic blood flow have not proved very helpful in assessing the individual patient, as there is a wide overlap of normal values with those obtained in cirrhotic patients. In the occasional patient found to have a very low hepatic blood flow, it would seem unwise to divert further portal blood from the liver by operation.

The main aim of the studies at present being undertaken is the assessment of patients with cirrhosis of the liver. It is hoped that the selection of patients for shunt operations will become more logical and that earlier operations will be carried out on more suitable patients.

Methods Available for the Estimation of Portal Pressure and Hepatic Blood Flow in Man.

Portal Pressure.

Direct measurement of portal pressure is regularly carried out during operations on patients with portal hypertension and may be possible by percutaneous needling of the portal vein, which has been carried out by Bierman, Steinbach, White and Kelly (1952).

Measurement of venous pressure in collaterals has been carried out in dilated abdominal wall veins (Davidson, Gibbons and Faloon, 1950), in hæmorrhoids and in œsophageal varices (Allison, 1951; Palmer, 1951).

Recently Atkinson and Sherlock (1954) have used a lumbar puncture needle inserted percutaneously to measure intrasplenic pressure.

The estimation of pulmonary capillary pressure by Hellems, Haynes, Gowdey and Dexter (1948) from the pressure in an occluded pulmonary arteriole suggested to Myers and Taylor (1951) that the pressure in an hepatic venule might give an indication of portal venous pressure. A catheter was passed via the median cubital vein into an hepatic vein as suggested by Warren and Brannon (1944), and the tip was advanced until it was arrested by the walls of a venule near the periphery of the liver. The pressure of the motionless column of blood in the occluded venule was then recorded. The technique and rationale of this procedure have been discussed by Paton, Reynolds and Sherlock (1953) and by Krook (1953). Paton *et alii* conclude that, in the absence of extrahepatic portal obstruction, the occluded hepatic venule pressure is representative of the pressure in the portal system, and this pressure does not differ significantly from that obtained directly from a portal vein radicle by means of polythene tubing left *in situ* after operation. Reynolds *et alii* (1954) have also made simultaneous pressure readings, from the portal vein and occluded hepatic venule, and they state that occluded hepatic venule pressure has proved of great value in assessing the need for portacaval surgery in patients with cirrhosis and gastro-intestinal bleeding.

Hepatic venule catheterization has been the method used in the cases reported in this series. The portal pressure has been measured directly at operation in the only patient treated surgically.

Hepatic Blood Flow.

The introduction of hepatic vein catheterization by Warren and Brannon (1944) made possible the collection of samples of hepatic vein blood. Indirect estimation of hepatic blood flow in man by means of the Fick principle was first carried out by Bradley, Ingelfinger, Bradley and Curry (1945), who determined bromsulphalein extraction.

In 1947 Lipscomb and Crandall, employing the same principle, estimated hepatic blood flow in dogs from urea production. Both methods have been used in human subjects by Myers (1947), who concluded that, although the figures obtained were comparable, the urea procedure was more tedious and open to far greater inaccuracy than the bromsulphalein method.

The indirect method with the use of bromsulphalein has been shown to give a reliable measure of hepatic blood flow in anæsthetized dogs by Selkurt (1954), who obtained simultaneous direct measurements under varying physiological conditions by leading off the venous outflow from the liver between balloons inflated in the inferior *vena cava* and returning the blood to an external jugular vein after it had passed through a volume recorder. The venous return from the lower part of the body was diverted through an external circuit to the other external jugular vein.

Recently Dobson, Warner, Finney and Johnston (1953) have used the disappearance rate of colloidal chromic phosphate to determine hepatic blood flow in normal man, a procedure which does not necessitate catheterization of an hepatic vein. The results obtained in 29 normal young men were of the same order as those of Bradley *et alii* and of Myers by the bromsulphalein and urea methods. However, this method would appear open to fallacy when applied to patients with collateral circulation, as the spleen has been shown to remove a considerable proportion of the particles, and the method assumes hepatic blood flow to equal total splanchnic blood flow. This type of objection when applied to the bromsulphalein method is largely overruled by the attainment of a steady state of saturation of extrahepatic tissues, a condition which cannot be attained during an experiment to measure disappearance rates.

Estimation of hepatic blood flow has been by the technique of bromsulphalein extraction in the cases so far studied in this series.

Review of Normal Values and Previous Findings in Cirrhosis.

Portal Pressures.

The upper limit of normal for portal pressure measured directly at operation was regarded as about 150 millimetres of water, or 11 millimetres of mercury, by Walker (1952), though Gray (1951) regarded 210 millimetres of water (15·5 millimetres of mercury) as the upper limit.

The findings of Myers and Taylor (1951), of Paton, Reynolds and Sherlock (1953) and of Krook (1953) for occluded and free hepatic vein pressures in normal subjects are recorded in Table I. The upper limit of normal in the occluded position is thus about 12 millimetres of mercury. Values above 12 millimetres of mercury, in the presence of a steep gradient down to the pressure in the free hepatic vein, are reliable evidence of portal hypertension. When the pressure in the free hepatic vein is also high and approaches the occluded venule pressure, this is indicative of systemic venous congestion, as in congestive heart failure.

Table II records the findings of a number of workers using the methods previously cited to measure or estimate portal pressure in 125 patients with portal cirrhosis. There is very good agreement between the pressure ranges obtained by the five different methods, and there is almost no overlap of the pressures in patients with cirrhosis and those in normal subjects.

Hepatic Blood Flow.

Bradley, Ingelfinger and Bradley (1952) reported the findings for hepatic blood flow by the use of the bromsulphalein method in a series of 91 normal patients, and in a group comprising 35 patients with cirrhosis and four patients with extrahepatic portal obstruction (Table III). The overlap of values in normal and cirrhotic patients was great, and it would seem that only figures below 970 millilitres per minute can be regarded as definitely abnormal when an individual patient is being considered.

TABLE I.

Estimation of Portal Pressure by Hepatic Vein Catheterization. Previous Findings in Normal Subjects.

Authors.	Number of Cases.	Pressure. (Millimetres of Mercury.)			
		Occluded Hepatic Venule.		Free Hepatic Vein.	
		Mean.	Range.	Mean.	Range.
Myers and Taylor (1951)	12	4·8	—	3·3	—
Paton, Reynolds and Sherlock (1953) ..	24	6·8±0·49	2·6 to 11·2	4·9±0·46	0·6 to 10·6
Krook (1953)	10	6·4	3 to 10	4·0	2 to 6

Comments on the Techniques Employed in the Present Study.

All patients were studied in the post-absorptive state. In most instances no sedation was considered necessary, but nervous patients were given 1·5 grains of pentobarbital one hour beforehand. Portal pressure was estimated by measurements of the occluded hepatic venule pressure, and estimation of hepatic blood flow was by the bromsulphalein extraction technique. Hepatic vein catheterization is necessary for both procedures. A number eight Cournand cardiac catheter with single lumen and end hole was passed into one or more hepatic veins, usually from the right median cubital vein, with the aid of fluoroscopy. Pressures were measured with a strain gauge manometer, and its amplified output was recorded by a Sanborn Cardiette. All measurements were made relative to a point five centimetres below the sternal angle with the patient lying supine. The pressure in several occluded hepatic venules was recorded, each reading being followed by a reading with the catheter tip lying free in the corresponding hepatic vein.

TABLE II.

Measured or Estimated Portal Pressure in Cirrhosis of the Liver.

Observer.	Patients in Series.	Range of Pressures. (Millimetres of Mercury.)	Comment.
At Operation.			
Pattison (1949) ..	10	9 to 44	One patient with normal pressure.
Blakemore (1951) ..	18	18 to 45	
Walker (1952)	21	15 to 41	Patients with œsophageal bleeding.
	7	10 to 27	Patients with ascites.
In Œsophageal Varices.			
Palmer (1954)	15	17 to 38	
In Abdominal Collaterals.			
Davidson, Gibbons and Faloon (1950) ..	10	18 to 34	
Intraspienic.			
Atkinson and Sherlock (1954)	16	17 to 35	
Occluded Hepatic Venule.			
Myers and Taylor (1951)	7	11·5 to 32	
Paton, Reynolds and Sherlock (1953) ..	11	15·6 to 35·2	
Krook (1953)	10	12 to 27	

For the estimation of hepatic blood flow the technique described by Bradley *et alii* (1945) was carried out, with the catheter tip lying free near the centre of the right hepatic lobe. A calibrated Murphy's drip and tunnel clamp was used and the bromsulphalein infusion maintained at a known constant rate. It is desirable to maintain a steady peripheral plasma level of bromsulphalein between 1·0 and 4·0 milligrammes per 100 millilitres (Sherlock, Bearn, Billing and Paterson, 1950), though in the present studies the level varied from 0·5 to 4·3 milligrammes per 100 millilitres. Results were discarded if this level was changing at a rate of more than 0·02 milligramme per 100 millilitres per minute. After at least thirty minutes from the commencement of the infusion had been allowed for stabilization, blood samples were collected at ten-minute intervals from peripheral and hepatic veins simultaneously, for a minimum of thirty minutes. Dry syringes were used and the blood was transferred to tubes containing dry heparin. The separated plasma was stored in a refrigerator for not more than four days before the result was read. Bromsulphalein levels were read in duplicate in a Beckman spectrophotometer at 580 and 620 millimicrons as described by Gaebler (1945). Optical density was found to change very quickly after the addition of alkali, and each sample was prepared immediately before the reading.

TABLE III.

Estimated Hepatic Blood Flow in Normal Subjects and Cirrhotics. (Bradley, Ingelfinger and Bradley (1952).)

Subjects.	Estimated Hepatic Blood Flow. (Millilitres per Minute.)	Range. (Millilitres per Minute.)
91 normal subjects ..	1530±300	970 to 2370
39 cirrhotics[1]	1090±380	480 to 1990

[1] Including four cases in which extrahepatic portal obstruction was present.

Estimated hepatic plasma flow was calculated by dividing the removal rate (R) of bromsulphalein by the difference between afferent (peripheral vein) and efferent (hepatic vein) plasma levels (P–H). The removal rate of bromsulphalein was obtained from the infusion rate, which it equalled when the peripheral plasma level was constant. Estimated hepatic blood flow ($EHBF$) was obtained by multiplying the plasma flow by $\frac{1}{1-Ht}$ where Ht was the hæmatocrit of hepatic vein blood. Thus

$$EHBF = \frac{R}{P-H} \times \frac{1}{1-Ht}.$$

The derivation of this equation and the assumptions involved have been discussed in detail by Bradley *et alii* (1945).

Results and Discussion.

The results of 25 studies on 23 patients form the basis of this report. Occluded hepatic venule pressures have been recorded in all cases, in 10 of which estimation of hepatic blood flow has also been carried out. Only one patient has been treated surgically, and his splenic vein pressure was measured directly at operation (Table IV).

TABLE IV.

Case No.	Patient's Sex.	Age. (Years.)	Findings on Liver Biopsy.	Varices.	Splenomegaly.	Pressure. (Millimetres of Mercury.) OHV.[1]	Pressure. (Millimetres of Mercury.) FHV.[1]	EHBF. (Millilitres per Minute.)	Clinical Features.
Cirrhosis of the Liver.									
1	M.	53	Marked fibrosis, gross distortion.	Yes.	+++	26	1	930	Hæmochromatosis, jaundice.
2	F.	35		Yes.	++	25	10	1250	Ascites, hepatic coma, death.
3	M.	32	Marked fibrosis.[2]	No.	+++	23	4	—	Well; ankle œdema.
				Yes.	++	24	3	1640	(Six months later.)
4	F.	54	Marked fibrosis, gross distortion.	Yes.	+	20	0	—	Ascites, hæmorrhage, coma, death.
5	M.	56		Yes.	+	19	4	—	Ascites, hepatic pre-coma.
6	M.	53	Marked fibrosis, gross distortion.	Yes.	—	15	0	—	Hæmorrhage, coma, death[3] (1954).
7	F.	62	Marked fibrosis, gross distortion.	No.	—	14	2	—	Jaundice.
8	M.	12	Marked fibrosis.[2]	No.	++	13	5	—	Well.
9	F.	32	Moderate fibrosis.[2]	No.	+	12	3	—	Jaundice.
10	M.	37	Moderate fibrosis.[2]	No.	—	10	1	—	Jaundice.
11	M.	31	Moderate fibrosis.[2]	No.	—	8	5	1350	Well.
12	M.	38	Marked fibrosis, gross distortion.	No.	—	7	2	1540	Gout, cinchophen given, jaundice.
13	M.	53	Moderate fibrosis, little distortion.	No.	+	5	3	—	Intercurrent infection, death.
14	M.	71	Moderate fibrosis.[2]	No.	+	4	2	—	Malaise.
15	F.	49	Moderate fibrosis.[2]	No.	—	3	0	1330	Jaundice.
16	M.	52	Moderate fibrosis, periportal.	No.	—	2	0	—	Pneumonia, stupor.
Cirrhosis with Portal Vein Thrombosis.									
17	M.	49	Marked fibrosis, gross distortion.	Yes.	++	6 10	5 5	1300 735	Hæmorrhage, spleno-renal shunt.[4] Three weeks after operation.
Miscellaneous Group.									
18	M.	37	Chronic venous congestion.	—	—	10	10	—	Valvular heart disease.
19	M.	62	Normal liver.	—	++	10	2	—	Hodgkin's disease.
20	M.	42	——	—	+	9	4	—	Alcoholic peripheral neuritis.
21	M.	39	——	No.	—	8	4	1600	Alcoholic peripheral neuritis.
22	M.	43	——	—	—	5	3	1080	Alcoholic peripheral neuritis.
23	M.	32	Normal liver.	No.	++	4	2	2070	Acquired hæmolytic anæmia.

[1] OHV = occluded hepatic venule; FHV = free hepatic vein.

[2] Architecture uncertain.

[3] Hepatic artery ligation, 1951.

[4] Splenic vein pressure at operation, 31 millimetres of mercury.

For the purposes of this discussion, cirrhosis of the liver has been regarded as synonymous with hepatic fibrosis.

Occluded Hepatic Venule Pressures.

The occluded hepatic venule pressure was normal in a miscellaneous group of six patients who were suffering from alcoholic peripheral neuritis (three patients), hæmolytic anæmia (one), Hodgkin's disease (one) and rheumatic heart disease (one).

The remaining 17 patients were suffering from cirrhosis of the liver. The diagnosis was proved histologically in all but two patients, both of whom presented the clinical features of advanced cirrhosis. One of the patients with cirrhosis also had portal vein thrombosis, demonstrated by splenography, and was the only patient in the present series on whom a shunt operation was performed (a spleno-renal anastomosis by Dr. J. I. Loewenthal). As expected, his hepatic venule pressures before and after operation were normal and the splenic vein pressure at operation was high (31 millimetres of mercury).

This leaves for consideration 16 patients with hepatic cirrhosis, in eight of whom occluded hepatic venule pressure was found to be above the upper limit of normal (12 millimetres of mercury); pressures in the remaining eight patients were within the normal range (Table IV).

Previous reports of portal pressure measurement or estimation in cases of cirrhosis (Table II) may be divided into two groups according to the methods employed: (*a*) measurement of pressure in collaterals or direct measurement at operation, when the raised portal pressure has already been revealed clinically by the presence of the collaterals or by œsophago-gastric hæmorrhage; (*b*) measurement of hepatic venule or intrasplenic pressure, when the patient does not necessarily present clinical evidence of portal hypertension.

It is not surprising that the reports in group (*a*) are of pressures almost exclusively above the normal range; but it is remarkable that in group (*b*) there is almost no overlap of the pressures in 44 patients with cirrhosis and those found in normal controls. Krook's studies included four patients "with liver disease" whose pressures were at the upper limit of normal, but the presence or absence of hepatic fibrosis was not specified. So far almost every patient with definite hepatic fibrosis who has been studied and reported has been shown to have portal hypertension.

This creates the impression that portal pressure is above normal in all patients with cirrhosis of the liver. It implies the rarity or non-existence of (i) an early phase of cirrhosis during which the portal pressure may still be within normal limits, and (ii) a quiescent inactive hepatic fibrosis without portal hypertension. This impression has probably been created accidentally by case selection and the desire to demonstrate clearly the value of the methods employed.

In the present study the patients in the cirrhotic group were selected on histological grounds, with the exception of the two patients already mentioned. Thus in the majority of these cases the selection was made irrespective of the presence or absence of the clinical features of cirrhosis. The estimated portal pressure was above normal in only eight of the 16 patients. The low pressures obtained are believed to be a true representation of portal pressure, and not the result of faulty technique, for the following reasons: (i) Great care was taken to obtain readings from several sites and to avoid arrest of the catheter at venous bifurcations, which is a well-recognized source of error. (ii) Varices have been demonstrated radiologically in six of the patients with raised pressure, but in none of the patients with normal pressure. (iii) There is a striking contrast between the clinical features of the two subgroups: hæmorrhage, ascites, hepatic coma and death in the portal hypertensive group, and in the other group

malaise and transient jaundice the only symptoms, if any. One patient in the second group died from an illness apparently unrelated to his liver disease.

Another possible explanation of normal pressure readings in the hepatic venule would be the presence of secondary portal vein thrombosis. Though splenography and measurement of intrasplenic pressure have not been carried out in these cases, the presence of secondary portal vein thrombosis in any of the group with normal pressure appears most unlikely in the absence of varices and gross splenomegaly.

It is of interest, in the light of previous findings, that a normal estimated portal pressure has been found in patients with hepatic fibrosis as often as the more classical picture of fully developed or rising portal hypertension.

Comparison of these results with the histological findings suggests that most patients with severe hepatic fibrosis have raised portal pressure, while those with moderate fibrosis frequently have not. The correlation between portal pressure and hepatic architecture suggested by Walker (1952) was not observed, but many of the needle biopsy specimens were not large enough for the architecture to be defined.

Estimated Hepatic Blood Flow.

The hepatic blood flow was estimated in ten patients; six of them were suffering from cirrhosis of the liver, one from cirrhosis with portal vein thrombosis, two from alcoholic peripheral neuritis, and one from hæmolytic anæmia.

The results (Table IV) fall within the appropriate ranges found by Bradley *et alii* (1952) for patients with and without cirrhosis (Table III). The only features of particular interest are the fall from 1300 millilitres per minute to 735 millilitres per minute after spleno-renal shunt in the patient already mentioned, and the rather high figure of 2070 millilitres per minute in the patient with hæmolytic anæmia, who had an enlarged spleen and a normal liver. The figure of 930 millilitres per minute in the patient with the highest estimated portal pressure is well within the range for cirrhotics found by Bradley *et alii*, but the flow would be expected to fall to about 600 millilitres per minute if a porta-systemic shunt was constructed (Bradley, Smythe, Fitzpatrick and Blakemore, 1953). This problem will be considered in the next section.

The remaining results obtained for hepatic blood flow have not proved of any practical value in the diagnosis or prognosis of the individual patient.

Comment.

The aim cited in the opening section of this report was the assessment of patients with cirrhosis of the liver, and in particular the earlier and more logical selection of patients for shunt operation. In the 17 cases of cirrhosis of the liver portal hypertension has been found less often than was initially expected, and only one patient has so far been submitted for operation. Of the other eight patients with portal hypertension, two have had pressures only slightly above normal and no œsophageal varices, and four have had strong contraindications to operation—notably episodes of hepatic coma or pre-coma. The other two patients will be discussed in more detail.

CASE 1.—The patient suffers from primary hæmochromatosis with mild diabetes (Table IV). He has gross cirrhosis with pronounced distortion of hepatic architecture, a low hepatic blood flow (930 millilitres per minute) and a high portal pressure (occluded hepatic venule pressure 26 millimetres of mercury). Multiple œsophageal varices have been demonstrated by X-ray examination with barium, but he has not yet suffered from a gastro-intestinal hæmorrhage. In the last three months he has developed jaundice which is still present, despite prolonged bed rest. Though this patient presents some indications for shunt operation, there are several factors against such a procedure at present. The combination of a low hepatic blood flow, diabetes, and some evidence of hepatic decompensation in the form of jaundice, strongly contraindicates operation, and the decision to operate has been postponed to allow further observation of the progress of his disease.

CASE 3.—The patient has chronic active hepatitis with œdema and high thymol and zinc sulphate turbidity (Table IV). Liver biopsy reveals pronounced hepatic fibrosis, his hepatic blood flow is normal (1640 millilitres per minute), the occluded hepatic venule pressure is high (24 millimetres of mercury), and although there has been no significant increase in this pressure during the past six months, œsophageal varices have appeared during the same period. He has not yet suffered from a gastro-intestinal hæmorrhage. If and when the activity of his hepatitis abates, this patient will be seriously considered as a candidate for surgery.

Thus 17 patients with cirrhosis have been assessed and one spleno-renal shunt has been performed, with a successful outcome during a follow-up period of six months. Two further candidates have been rejected at least temporarily pending improvement in hepatic function. Three of the patients have died in hepatic coma, and one has died from an unrelated illness.

Follow-up studies on all available patients will be carried out as far as possible.

Summary.

The desirability of estimating portal pressure and hepatic blood flow in man has been discussed, and the available methods and previous findings in patients with and without cirrhosis of the liver have been reviewed.

Catheterization of hepatic veins has been performed in 23 cases; 17 of the patients were suffering from cirrhosis of the liver. Portal pressure has been estimated by measuring occluded hepatic venule and free hepatic vein pressures in all the patients studied, and hepatic blood flow has been estimated on eleven occasions by means of the method of bromsulphalein extraction.

The estimated portal pressure was normal in half of the patients with cirrhosis, and this has been stressed in the light of the findings of previous investigators.

No conclusions have been drawn from the values obtained for hepatic blood flow, which have been in agreement with those previously reported.

Comment has been made on the progress of the clinical programme of which these investigations form a part.

Acknowledgements.

The writer is indebted to Dr. C. R. B. Blackburn, Director of the Clinical Research Unit, for his helpful guidance and criticism; to Dr. B. Sinclair-Smith and the staff of the Hallstrom Institute of Cardiology for their cooperation and the use of the fluoroscopy room and recording apparatus; and to Sister M. Helsen and Mr. G. W. Latham for patient assistance and technical advice. He wishes to thank the members of the honorary staff of the Royal Prince Alfred Hospital who have given permission for their patients to be included in this study.

References.

ALLISON, P. (1951), "The Measurement of Blood Pressure in Esophageal Varices", *Thorax*, 6: 325.

ATKINSON, M., and SHERLOCK, S. (1954), "Intrasplenic Pressure as Index of Portal Venous Pressure", *Lancet*, 1: 1325.

BIERMAN, H. R., STEINBACH, H. L., WHITE, L. P., and KELLY, K. H. (1952), "Portal Venipuncture. A Percutaneous, Trans-hepatic Approach", *Proc. Soc. Exper. Biol. & Med.*, 79: 550.

BLAKEMORE, A. H. (1951), "Portacaval Shunt for Portal Hypertension. Follow-up Results in Cases of Cirrhosis of the Liver", *J.A.M.A.*, 145: 1335.

BRADLEY, S. E., INGELFINGER, F. J., BRADLEY, G. P., and CURRY, J. J. (1945), "The Estimation of Hepatic Blood Flow in Man", *J. Clin. Investigation*, 24: 890.

BRADLEY, S. E., INGELFINGER, F. J., and BRADLEY, G. P. (1952), "Hepatic Circulation in Cirrhosis of the Liver", *Circulation*, 5: 419.

BRADLEY, S. E., SMYTHE, C. M., FITZPATRICK, H. F., and BLAKEMORE, A. H. (1953), "The Effect of a Portacaval Shunt on Estimated Hepatic Blood Flow and Oxygen Uptake in Cirrhosis", *J. Clin. Investigation*, 32: 526.

DAVIDSON, C. S., GIBBONS, T. B., and FALOON, W. W. (1950), "Systemic and Portal Venous Pressures in Cirrhosis of the Liver", *J. Lab. & Clin. Med.*, 35: 181.

DOBSON, E. L., WARNER, G. F., FINNEY, C. R., and JOHNSTON, M. E. (1953), "The Measurement of Liver Circulation by Means of the Colloid Disappearance Rate. I. Liver Blood Flow in Normal Young Men", *Circulation*, 7: 690.

GAEBLER, O. H. (1945), "Determination of Bromsulphalein in Normal, Turbid, Hemolyzed or Icteric Serums", *Am. J. Clin. Path.*, 15: 452.

GRAY, H. K. (1951), "Clinical and Experimental Investigation of the Circulation of the Liver", *Ann. Roy. Coll. Surgeons England*, 8: 354.

HELLEMS, H. K., HAYNES, F. W., GOWDEY, J. F., and DEXTER, L. (1948), "Pulmonary Capillary Pressure in Man", *J. Clin. Investigation*, 27: 540.

KROOK, H. (1953), "Estimation of Portal Venous Pressure by Occlusive Hepatic Vein Catheterization", *Scandinav. J. Clin. & Lab. Investigation*, 5: 285.

LIPSCOMB, A., and CRANDALL, L. A. (1947), "Hepatic Blood Flow and Glucose Output in Normal Unanæsthetised Dogs", *Am. J. Physiol.*, 148: 302.

MYERS, J. D. (1947), "Hepatic Blood Flow and Splanchnic Oxygen Consumption of Man. Their Estimation from Urea Production or Bromsulphalein Extraction during Catheterisation of Hepatic Veins", *J. Clin. Investigation*, 26: 1130.

MYERS, J. D., and TAYLOR, W. J. (1951), "An Estimation of Portal Venous Pressure by Occlusive Catheterisation of an Hepatic Venule", *J. Clin. Investigation*, 30: 662.

PALMER, E. D. (1951), "Determination of Venous Pressure within Esophageal Varices", *J.A.M.A.*, 147: 570.

PALMER, E. D. (1954), "Effect of the Valsalva Maneuver on Portal Hypertension in Cirrhosis", *Am. J. M. Sc.*, 227: 661.

PATON, A., REYNOLDS, T. B., and SHERLOCK, S. (1953), "Assessment of Portal Venous Hypertension by Catheterisation of Hepatic Vein", *Lancet*, 1: 918.

PATTISON, A. C. (1949), "Use of Portacaval Anastomosis in Portal Cirrhosis", *Arch. Surg.*, 58: 590.

REYNOLDS, T. B., BALFOUR, D. C., JUNIOR, LEVINSON, D. C., MAGIDSON, O., MIKKELSEN, W. P., and PATTISON, A. C. (1954), "Measurement of Portal Venous Pressure by Hepatic Vein Catheterisation", *Am. J. Med.*, 17: 124.

SELKURT, E. E. (1954), "Comparison of the Bromsulphalein Method with Simultaneous Direct Hepatic Blood Flow", *Circulation Res.*, 2: 155.

SHERLOCK, S., BEARN, A. G., BILLING, B. H., and PATERSON, J. C. S. (1950), "Splanchnic Blood Flow in Man by the Bromsulphalein Method. The Relation of Peripheral Plasma Bromsulphalein Level to the Calculated Flow", *J. Lab. & Clin. Med.*, 35: 923.

WALKER, R. M. (1952), "The Pathology and Treatment of Portal Hypertension", *Lancet*, 1: 729.

WARREN, J. V., and BRANNON, E. S. (1944), "A Method of Obtaining Blood Samples Directly from the Hepatic Vein in Man", *Proc. Soc. Exper. Biol. & Med.*, 55: 144.

RUPTURE OF THE SPLEEN.

By J. L. CONNELL, M.S., F.R.C.S., F.R.A.C.S.,
Melbourne.

THE first successful splenectomy for rupture of the spleen was performed in 1892 (Roettig, 1943). In this report I shall confine my remarks to rupture of the normal spleen. Traumatic damage to a diseased spleen, although a common event in the Orient, is rarely met with in this country or in England.

In all subcutaneous injuries to the abdomen the spleen is the most commonly damaged organ (Roettig, 1943; McIndoe, 1932). The spleen lies in a well-protected position in the body and the frequency of its rupture must be attributed to the following factors: (i) The friable nature of the organ. (ii) The fact that it lies suspended by the lieno-renal and gastro-splenic ligaments and is quite mobile. It can be very easily moved by direct or indirect violence. It may be thrown against the vertebral column and is most susceptible to damage by *contre coup* (McIndoe, 1932). (iii) The fact that the convex surface of the spleen is closely applied to the thoracic cage, and any damage to the overlying ribs will often rupture it.

The splenic artery is the second largest artery supplying an abdominal viscus (the renal is the largest). The spleen itself is virtually a blood lake. Any tear in this organ therefore usually gives rise to alarming hæmorrhage. As a rule the closer the tear to the hilum, and therefore the larger the artery involved, the more profuse the bleeding.

The force required to rupture a normal spleen is usually considerable (McIndoe, 1932; Bailey, 1930), and indeed the condition is most usually caused by a motor-car accident, the accident frequently producing associated injuries.

Types of Injuring Force.

The types of injuring force are as follows: (i) direct force to the lower ribs and left hypochondrium; (ii) indirect force—for example, a fall from a height; (iii) blast injuries, of which Gordon-Taylor wrote during World War II; (iv) direct penetrating wounds; these are not common, and as a rule the injury to the spleen is obvious and presents no diagnostic problem.

There are, however, undoubtedly cases in which the trauma has been of a very minor nature, and others in which apparently there has been no trauma at all (spontaneous rupture). There appears to be no relationship between the force of the injury and the degree of bleeding.

The tears in the spleen may be on the convex or concave surface and may or may not extend across the hilum. The spleen may be rent in two or several pieces, or there may be no external rent, the hæmorrhage being entirely confined to the organ, as either a parenchymal or a subcapsular hæmatoma. The hæmorrhage may be catastrophic, usually in cases of a tear across the hilum or one completely severing the spleen from its pedicle. These patients progress rapidly to profound shock, and the mortality is very high. Usually, however, the bleeding is not as torrential as this, and one has a chance to diagnose and treat the condition.

Clinical Picture.

Rupture of the spleen may present clinically in a variety of ways, as follows: (i) primary rupture, (ii) delayed clinical manifestations, (iii) minor rupture with spontaneous healing.

In the primary rupture group hæmorrhage from the spleen is immediate and continuous. The patients are admitted to hospital in a few hours, the condition is diagnosed and they are operated upon. They plainly have suffered an intraabdominal catastrophe and usually display obvious signs of internal hæmorrhage. This is the commonest group, and in Larghero's series formed 76·8% of the cases. It is, of course, obvious that the severity of these cases is directly dependent upon the extent of bleeding; some are so severe that the patient succumbs before treatment can be given.

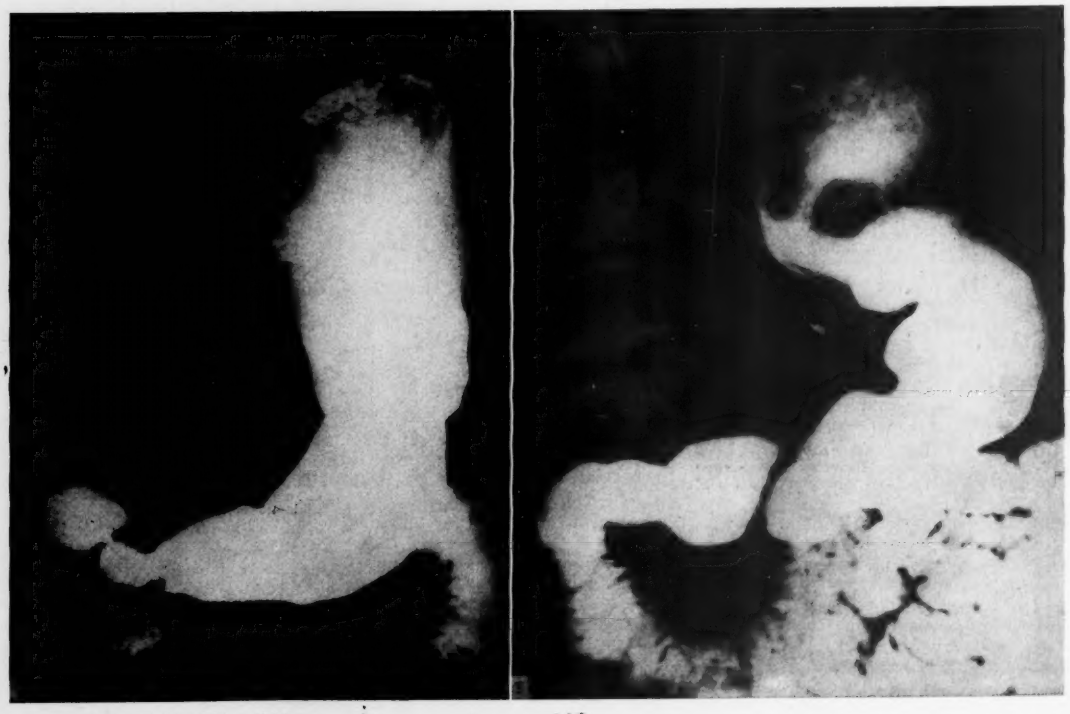
In the second group there is a history of injury which usually produces a shocked state. The patient more or less quickly recovers from this, and, apart from soreness over the lower left ribs, his condition is good, provided that there are no more serious associated injuries. This group then falls into two subdivisions: (*a*) Symptoms and signs of shock and intraabdominal injury return in a few hours, either slowly and progressively or very suddenly. The diagnosis becomes obvious, at least as an abdominal catastrophe requiring urgent surgical intervention. (*b*) The patient remains more or less asymptomatic for days, weeks or months, and then suddenly there is secondary bleeding from the damaged spleen, producing obvious symptoms and signs. This is the now well-known group of delayed hæmorrhage. This subject will be discussed fully later, when an illustrative case will be presented. This large group, the feature of which is the delayed onset of serious symptoms and signs, forms about 20% of cases of rupture of the spleen.

The last group comprises those cases in which the splenic bleeding does not give rise to sufficient signs to merit laparotomy. In other words, they are cases of minor rupture of the spleen in which the diagnosis is not made, the laceration heals and spontaneous cure occurs.

Roettig *et alii* (1943) doubt whether spontaneous cure of a splenic rupture ever occurs. Webb (1940) draws attention to the fact that Professor McCartney, of the University of Minnesota, reviewed 25,000 autopsy reports without finding evidence of a healed rupture of the spleen. On the other hand, Gordon-Watson (1932) describes two pathological specimens in the museum of Saint Bartholomew's Hospital which show just such healing. Susman (1927) is convinced that at least temporary, if not permanent, healing must occur at times.

ILLUSTRATIONS TO THE ARTICLE BY J. L. CONNELL, M.S., F.R.C.S., F.R.A.C.S.

ILLUSTRATIONS TO THE ARTICLE BY KENNETH W. STARR.



ILLUSTRATIONS TO THE ARTICLE BY BRIAN L. MARKS.

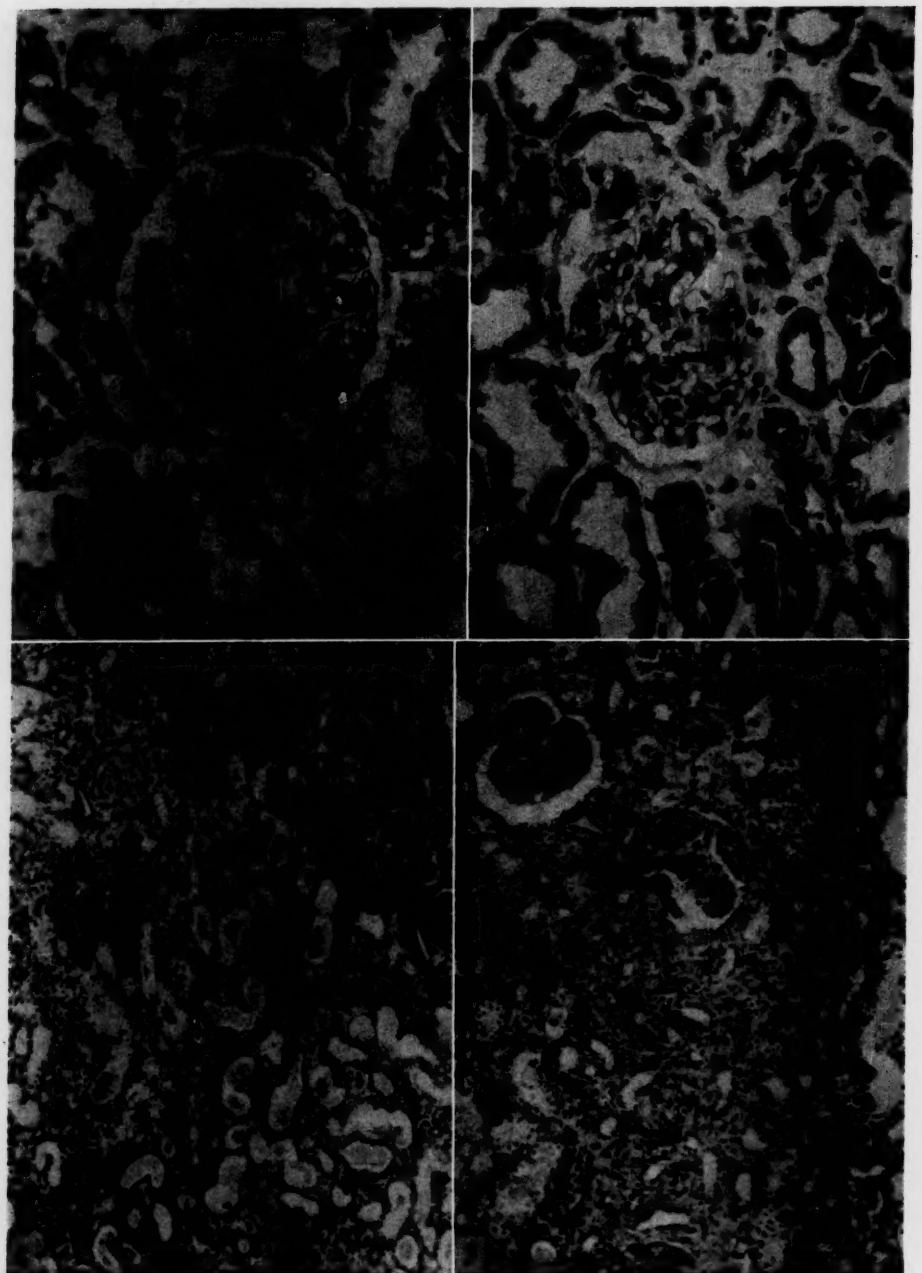


FIGURE I.—Section of biopsy specimen showing an essentially normal glomerulus (×288). FIGURE II.—Section of biopsy specimen, the only abnormality being slight arteriolar thickening (×288). FIGURE IV.—Section of left kidney showing casts and cellular infiltration (×104). FIGURE V.—Section of left kidney showing adhesion of tufts (×144).

I think it logical to assume that some rents in the spleen give rise to only a small hæmatoma when the bleeding is stopped before it reaches clinical proportions. After all, McCartney's review of autopsy reports may not mean much. If a spleen had been ruptured years before, it might show very little evidence of damage at autopsy. There might be a small white scar and a few adhesions in the perisplenic bed. How often has one seen this accepted as within normal limits, both in the autopsy room and on the operating table! Let us consider the following case.

CASE I.—A., a greengrocer, aged thirty-nine years, presented to the out-patient department on March 17, 1953, with a story of having felt off colour for the past six weeks. He complained of pain in the epigastrium and left hypochondrium, increasing anorexia, loss of energy and weight, and attacks of shivering and sweating, particularly in bed at night. He had noticed of late that deep breathing and coughing accentuated his abdominal pain. He had had no previous illness and had never suffered from dyspepsia.

On examination he was a thin, pale man, obviously unwell. His skin was moist and clammy and his tongue coated and dry. His pulse rate was 100 per minute and his temperature 100·6° F. There was some diminution of percussion note and diminished air entry at the base of the left lung. In the abdomen there was moderate tenderness in the epigastrium and left hypochondrium, maximal in the left side of the epigastrium. No mass was palpable and there was no real rigidity, although the patient vigorously resented palpation high in the left epigastrium. The percussion note was normal over the region of tenderness, and there was no suggestion of increased splenic dulness.

He was admitted to hospital. An X-ray examination of his chest revealed no gross changes in the lungs, but obvious elevation of the left half of the diaphragm. He was examined under the fluoroscopic screen and the left side of the diaphragm failed to move with respiration. A blood examination gave the following results: the hæmoglobin value was 80% and the erythrocytes numbered 4,000,000 per cubic millimetre; the leucocytes numbered 32,000 per cubic millimetre, and gross polymorphonuclear leucocytosis was present.

A diagnosis of subphrenic abscess was made. He was given a course of penicillin and "Aureomycin", and although the initial response was dramatic, pyrexia and toxæmia recurred in five days. It was decided therefore to drain the abscess. A left paramedian incision was made and an opening was made into a large cavity filled with pus. The abscess lay to the front and left of the fundus of the stomach. A pint of pus was aspirated, and then about 20 ounces of old blood clot protruded upwards from the bottom of the cavity. The abscess was about six inches by six inches by six inches in size, and extended downwards between the stomach and spleen. The cavity was drained through a stab incision, and convalescence was smooth and rapid. He was discharged home a month after his admission to hospital. On the patient being questioned after the operation, he admitted to having had a severe fall on his left side from the back of a truck some months before. This fall produced extreme soreness over the left lower ribs for three or four days, but this gradually wore off. He did not stop work at any time.

I venture to suggest that had the blood clot in this case never become infected the patient would never have come to surgery. Perhaps an autopsy performed thirty years later would have revealed a normal-sized spleen "with moderate surrounding adhesions attached to the capsule".

The Diagnosis.

A ruptured spleen may produce a great variety of clinical symptoms and signs. These are never all present in any one case, but I think a full discussion of all the features that may occur is necessary. Apart from those cases in which torrential hæmorrhage occurs, the high mortality of ruptured spleen is due to failure to make a prompt diagnosis and therefore to delay in treatment.

There is nearly always a history of injury. This is most often a blow over the lower ribs on the left side. Frequently fractured ribs are present. However, the force may be applied anywhere to the abdomen, or it may be due to a fall from a height. A definite injury may be entirely absent from the history. There is no doubt, in my opinion, that spontaneous rupture of a normal spleen does occur. This will be discussed more fully later.

When the patient is first injured, shock is usually produced. Early this may be very severe. Such patients are often pale, with a weak, thready pulse, and syncope at this stage has often been reported. As was pointed out above, this shocked state usually continues and progresses; but in a significant number of cases (20% to 30%) there is a temporary recovery. Often when the patients are admitted to hospital the blood pressure and pulse rate are normal, and may remain so for some hours, despite continuous bleeding (Coleman, 1939). This is merely a manifestation of vasomotor defence, and one must not be lulled into a sense of security by these findings. The collapse from this state is often dramatic and profound, and the mortality of operation is very much higher after such a collapse than before (McIndoe, 1932).

Pain is invariably present (McIndoe, 1932; Roettig, 1943; Susman, 1927; Larghero, 1951). It can vary from a dull ache to a most excruciating agony which gives the patient no peace, and often forces him to draw his knees up to his abdomen. Although one would expect the pain to be maximal in the left upper quadrant of the abdomen, this is by no means always the case. Frequently it is generalized throughout the abdomen. It may be felt across the upper part of the abdomen with maximal severity in the epigastrium. The pain is often intermittent, or at least waxes and wanes in severity.

Kehr's sign consists of pain in the left shoulder tip. It is, of course, referred pain due to irritation of the central part of the diaphragm. It is present in only about 25% of cases (Roettig, 1943), and it has undoubtedly been given undue significance in the past. It is important to realize that if the sign is absent it may often be produced by tipping the patient into the Trendelenburg position for a few minutes. In two cases I have dealt with in which the abdomen was full of blood (one reported here (Case VI) and the other a case of ruptured ectopic gestation), Kehr's sign was not present, but there was severe pain in the back of the neck over the lower three cervical vertebræ. I have not seen this sign described before, but have no doubt that it has often been observed. Presumably this pain is also referred. Perhaps in these cases the diaphagm is innervated by lower cervical segments than usual.

Patients with pain in the shoulder or neck often sit up in bed to get relief. They state that the pain comes on only when they are in the supine position or is greatly accentuated by it. Frequently deep breathing will precipitate or enhance the pain.

Whilst we are discussing the subject of pain it is worth mentioning that some patients complain of discomfort in the rectum and tenesmus. This is due to blood in the pelvis, and of course peritoneal tenderness on rectal examination is often present and should always be looked for (Cases V and VII).

Pallor is almost constantly present and is a sign of great importance. It is the one sign which arouses suspicion of the diagnosis when the patient is first examined. Pallor is frequently present even though the blood pressure and pulse are normal.

The site of injury is important. A severe blow over the left lower ribs or left flank should always raise the possibility of ruptured spleen. Shallow hesitant breathing is suggestive of rib injury, and in these cases dulness and diminished air entry are often observed at the base of the left lung.

The blood pressure and pulse readings have been discussed earlier. Suffice it to say that the pulse may be rapid and thready and the blood pressure low, but normal readings by no means rule out the diagnosis. On the same premises there may or may not be air hunger.

Tenderness is always present in the abdomen, although sometimes this sign is minimal. There is usually considerable resistance to palpation of the abdomen, but rarely is true involuntary board-like rigidity present. These signs may be limited to the left upper quadrant or to the upper part of the abdomen, or be generalized. The importance of seeking pelvic peritoneal tenderness has been mentioned above.

If injury has occurred several hours before, it is not unusual to find the abdomen distended. This is not only due to fluid. Blood in the peritoneal cavity seems quickly to produce an atony of the gut, and of course paralytic ileus is a well-known complication of abdominal trauma (Larghero, 1951; McIndoe, 1932; Roettig, 1943; Bailey, 1930).

Increased dulness in the splenic area and in the left flank is a sign of great significance. With a suggestive history it makes the diagnosis. It is probably present in about 80% of cases (Roettig, 1943). Ballance's sign may be present—that is, dulness in both flanks, but the dulness in the right flank disappearing with change of position of the patient. Ballance's sign is reported as being present in about 25% of cases (Zabinski and Harkins, 1943).

It is always wise to examine the urine, for hæmaturia may be present. Damage to the left kidney is one of the most frequently associated injuries, and indeed is evidence that the injury received was severe enough to rupture the spleen (Larghero, 1951).

The blood should always be examined in doubtful cases, but I think it unwise to rely on this examination too much. It is well known that early after hæmorrhage the red cell count, hæmoglobin value and hæmatocrit readings may be normal. Hæmodilution has not yet occurred. Blood volume estimations are simply not practicable. A low red cell count and hæmoglobin value are of significance, of course, but usually the anæmia is evident on inspection of the patient in any case.

A plain X-ray film of the abdomen may be taken. Webb was the first to draw attention to the X-ray signs which may be evident with a ruptured spleen. These signs may be tabulated as follows: (*a*) increased density in the left hypochondrium; (*b*) elevation of the left leaf of the diaphragm; (*c*) displacement of the stomach to the right; (*d*) the presence of free fluid between loops of intestine. The X-ray films submitted from two of the cases reported in this article show, I think, signs of significance. In Figures II and V the gastric air bubble is displaced to the right. It is interesting to note that in both of these cases the gastric air bubble takes on a vertical crescent shape. This is not surprising in view of the intimate association of the two organs, and one can well imagine an expanding perisplenic hæmatoma indenting the fundus of the stomach and so distorting the gastric air bubble (Figure I).

If the diagnosis is obvious, it is unnecessary and unwise to take an X-ray film of the abdomen. However, in doubtful cases this can be a most helpful procedure.

Paracentesis abdominis is a feasible method of investigation. Wright and Prigott (1939) report 15 cases, in 13 of which blood was obtained from the peritoneal cavity on aspiration. It is as well to bear in mind that a false positive result may be obtained, and it is important to ignore a negative result. Penberthy and Reiners (1953) report a case in which fatal delay in treatment occurred because of a negative finding on *paracentesis abdominis*. As one must therefore discount a negative result, the test seems hardly worth while.

Associated Injuries.

Associated injuries in a patient with traumatic rupture of the spleen are reported in the literature as being present in 40% to 50% of cases. It is important to look for them, but far more important not to be dominated by them. The greatest danger of associated injuries is that they may cloud the surgeon's judgement, leading him to concentrate on the treatment of obvious injuries, whilst the patient dies of hæmorrhage from the spleen.

Wright and Prigot (1939), reporting 30 cases, found associated injuries present in half, and they list their findings as follows: (i) fractured ribs on the left side, ten cases; (ii) fracture of extremities, eight cases; (iii) lacerated left kidney, six cases; (iv) ruptured lung (hæmopneumothorax), four cases; (v) ruptured liver, three cases; (vi) injury to the brain, three cases; (vii) ruptured diaphragm, one case; (viii) ruptured bladder, one case.

Roettig *et alii* (1943) report an incidence of 46% associated injuries, and their classification is very similar to that listed above. It is rather surprising that in most statistics published there is no mention of associated damage to the pancreas, bowel or mesentery.

It is important to diagnose fractured ribs or lung injury, but it is far more important to realize that trauma causing these injuries may well have ruptured the spleen. It is rarely necessary to remove a lacerated kidney (Larghero, 1951), but it is vital to realize that a blow in the left flank producing hæmaturia may also have lacerated the spleen.

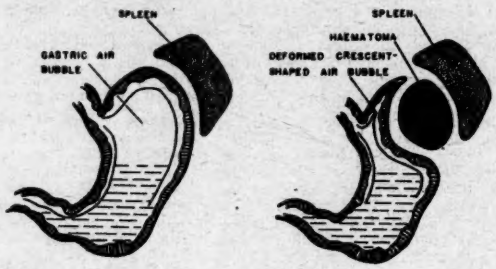


FIG 1A FIG 1B

FIGURE I.

Differential Diagnosis.

Ruptured spleen has often been misdiagnosed; Cases IV to VI reported here are examples. Most frequently the clinical picture has been attributed to: (i) fractured ribs or bruised muscles alone, (ii) ruptured intestine, (iii) ruptured liver, (iv) lacerated kidney alone, (v) perforated ulcer, (vi) ruptured ectopic gestation. (In (v) and (vi) this happens when the history of trauma is minimal.)

CASE II.—B, aged twenty-three years, was admitted to hospital on March 2, 1948. This patient, who had previously been well, fell and landed heavily on the left shoulder and loin eight hours before his admission. He experienced almost immediately sharp, stabbing pain in the left loin and pain in the tip of the left shoulder. He had also noticed persistent nausea since the fall.

On examination of the patient, he was in obvious pain, and considerable pallor of the skin and mucous membranes was evident. His breathing was easy. His blood pressure was 140 millimetres of mercury, systolic, and 80 millimetres, diastolic, and his pulse rate was 120 per minute. Pronounced tenderness was present over the tip of the left acromial process. Examination of the abdomen revealed considerable tenderness and rigidity in the left hypochondrium, spreading down to the left loin. There was increased dulness in the perisplenic area. No rectal examination was made. A confident diagnosis of traumatic rupture of the spleen was made, and this was confirmed at operation. Splenectomy was performed, and he was given a transfusion to replace his blood loss. Convalescence was completely uneventful, and he was discharged to a convalescent home on March 14.

The features to note about this case are the history of obvious trauma, the pallor, the shoulder tip pain, the site of abdominal pain, tenderness and rigidity, and the increase in splenic dulness.

CASE III.—C, aged twenty-seven years, was injured whilst playing football on the day of his admission to hospital (April 24, 1948). He received a severe blow on the left side. This temporarily winded him, but he recovered sufficiently to continue playing for another half-hour, until the game was over. Shortly afterwards he suddenly fainted, and on recovery complained of severe pain in the left hypochondrium and left loin. He vomited once. He was admitted to hospital five hours after injury.

On examination, the patient was lying quietly in bed, but pallor of the face was apparent. His blood pressure was 95 millimetres of mercury, systolic, and 70 millimetres, diastolic, but it shortly fell to 60 millimetres of mercury, systolic, and 40 millimetres, diastolic. The pulse rate was 92 per minute. Tenderness was present over the left lower ribs, in the hypochondrium and in the left loin. Increased dulness was noted in the splenic region, extending to the left loin. There was no rigidity. No rectal examination was

made. The hæmoglobin value was 77%. A blood transfusion was commenced, and his general condition quickly improved, the blood pressure rising to 120 millimetres of mercury, systolic, and 80 millimetres, diastolic, and the pulse rate dropping to 78 per minute. The pain and tenderness greatly diminished. Signs of shifting dulness developed in both flanks. Splenectomy for ruptured spleen was performed. During the splenectomy it was found that individual ligation of hilar vessels was impossible because of gross bleeding. He was discharged from hospital, fit and well, on May 4.

CASE IV.—D, aged forty-nine years, was admitted to hospital on November 10, 1949. On the day prior to his admission he was on a drinking bout and during this, at 10 p.m., he suddenly developed severe upper abdominal pain. He vomited shortly afterwards. During the next twelve hours the pain persisted, increased in severity, and became generalized over the abdomen. He had no shoulder tip pain.

On examination of the patient it was noticed that his complexion was pale and his breathing was hesitant and shallow. His temperature was 100·6° F. His blood pressure was 150 millimetres of mercury, systolic, and 100 millimetres, diastolic, and his pulse rate was 108 per minute. His abdomen did not move with respiration, and there was considerable tenderness in all quadrants and rigidity in the upper two. Shifting dulness was present in the flanks, but there was no evidence of any increase in splenic dulness. No rectal examination was made. The abdomen was examined under the fluoroscopic screen, and there was no gas under the diaphragm.

It was thought that the patient had general peritonitis, probably from a perforated ulcer. Laparotomy was performed and the abdomen was discovered to be full of blood. The spleen was grossly ruptured, but appeared to be otherwise normal. After operation the patient developed bilateral basal pulmonary collapse and a ruptured wound, which had to be sutured. Routine X-ray films of the chest displayed fractures of the fifth and sixth left ribs in the anterior axillary line.

There is no doubt that this is a case of traumatic rupture of the spleen. The patient was drunk and the trauma was either not felt or forgotten. It is interesting to note that, although there was no history of trauma, no satisfactory explanation was given before operation for the pallor which was evident on examination. The patient did have fractured ribs, and had they been discovered beforehand and the significance of the pallor realized, perhaps the correct diagnosis would have been made.

Delayed Rupture of the Spleen.

McIndoe was the first to discuss the problem of delayed rupture of the spleen when he reviewed 45 cases in 1932. Since then there have been numerous interesting papers, perhaps the most significant of which has been that by Zabinski and Harkins (1943), in which 177 cases are reviewed.

McIndoe laid down the maxim, which is now accepted, that for a case to be considered as one of delayed rupture there must be at least forty-eight hours between the injury and the collapse of the patient with signs of internal hæmorrhage. It is generally agreed that in all these cases bleeding has ceased, with the production of the latent period, and then it suddenly starts again.

In almost all cases there is some primary shock associated with the original injury. However, the patient quickly recovers from this, and his good clinical state usually dispels all doubts about a ruptured spleen. He may become completely asymptomatic, or have minimal complaints until the secondary hæmorrhage occurs, when he suddenly collapses.

All authorities are agreed that delayed rupture usually occurs in the first week (Zabinski and Harkins, 1943; Learmonth, 1951). McIndoe states that it is very rare indeed after the fourteenth day. Nevertheless, from time to time some extraordinary cases have been published, and latent periods of six months are now well recognized (Galvano and Lo Giudice, 1951). There are reports of intervals of eighteen months and even two years between the injury and the rupture, but they are doubtful (Zabinski and Harkins, 1943). In the case I shall report here there was a latent interval of eight weeks.

It seems that in these cases the original injury may produce the following results. (i) A perisplenic hæmatoma may form if bleeding ceases for any of several reasons. The hæmatoma may be confined by the stomach, colon, diaphragm and omentum sufficiently for enough pressure to be built up to stop the bleeding (McIndoe). A tag of omentum may become glued to the rent in the spleen and so give rise to the cessation of hæmorrhage. Alternatively, the clotting mechanism alone may be sufficient, in the circumstances, to cover the tear and stop oozing. (ii) An intraparenchymal hæmatoma is produced either beneath the capsule or within the splenic substance itself (Zabinski and Harkins, 1943; Ian Aird, 1949). Here again the bleeding ceases because of pressure. Such a hæmatoma may rupture later because (*a*) repeated small hæmorrhages occur, forcing the capsule to stretch more and more until it eventually gives way, or (*b*) the presence of the hæmatoma itself gives rise to autolysis, which is sufficient to soften the capsule enough for secondary rupture to occur.

Delayed hæmorrhage is a very serious matter and has a higher mortality than primary bleeding (Susman, 1927). This is due to the following two reasons as a rule: (i) Secondary hæmorrhage is usually fairly violent. Once the hæmatoma has broken through its constricting walls bleeding is usually very free. (ii) The patient has recovered from his setback after the injury, and by this previous experience both the patient and the surgeon are often persuaded to wait and see. There is no room for procrastination in such cases. It is interesting to note that in Case V, reported below, the patient refused operation for six hours after the diagnosis had been made.

More often than not a secondary rupture is produced by some minor strain such as lifting, coughing, sneezing or straining at stool. The secondary rupture in the case reported below was probably precipitated by bumps and jolts in the transport lorry. However, there have been many cases reported with no preceding strain. Indeed, many secondary ruptures have occurred whilst the patient was lying at rest in bed. Hueston (1951) reports its occurrence in a patient lying in bed recovering from a fractured femur, sustained at the time of injury.

The latent period between the original injury and the secondary rupture may be completely silent. The patient may be entirely asymptomatic, feel fit and well, and return to full activity. However, in a majority of cases, particularly in those in which a perisplenic hæmatoma is present, there are often very significant symptoms and signs. Most often the patient complains of aching pain in the left upper abdominal quadrant (McIndoe, 1932). This is usually not very severe, and often is intermittent. It rarely interferes with full activity. This pain may be accentuated by deep breathing. There may be a persistent elevation of the pulse rate and a mild pyrexia (McIndoe, 1932; Hueston, 1951). It is rare for the temperature to be greater than 100° F.

On examination of these patients one often finds persistent mild tenderness in the left hypochondrium. Splenic dulness is often increased, and indeed in some cases the spleen may be palpable, projecting beneath the left costal margin (McIndoe, 1932). The red cell count is usually within normal limits, but often there is a polymorphonuclear leucocytosis of over 20,000 cells per cubic millimetre (Zabinski and Harkins, 1943; Roettig *et alii*, 1943). In these cases, too, an X-ray examination of the abdomen may be of the greatest value.

It is possible then, in many cases, to make the diagnosis before secondary rupture of the spleen occurs. The advantages of so doing need hardly be emphasized. The important things are to be aware of the possibility and to watch carefully for the clinical signs outlined above (Larghero and Guiria, 1951).

CASE V.—E, a transport driver, aged forty years, was admitted to hospital on October 13, 1953. He said that half an hour previously he had suddenly experienced severe constant pain in the epigastrium, had become faint and nauseated, and shortly afterwards had noticed pain in both shoulder tips. On August 10, 1953, he had been involved in

a motor-car accident and as a result had been admitted to another hospital. Lacerations of the scalp, right hand and right elbow were treated. A report from the hospital stated that for a day, whilst he was under observation, it was thought that he might have internal bleeding. However, confirmatory signs were lacking, and after that his condition improved rapidly, and he was discharged home in a few days. He had had no other illness, and no symptoms of any kind since his discharge from the first hospital. During the day of his admission to hospital he had driven 100 miles in his motor lorry, but had sustained no injury of any kind.

On examination the patient lay curled up in bed, in obvious pain. His skin was pale, cold and clammy; the pallor was most obvious. His pulse rate was 80 per minute and his blood pressure 90 millimetres of mercury, systolic, and 60 millimetres, diastolic; this shortly rose to 105 millimetres of mercury, systolic, and 80 millimetres, diastolic. There was an impaired percussion note at the base of the left lung, and this extended forwards to the perisplenic region. Air entry was good at all areas. Examination of the abdomen revealed generalized tenderness, but this was most pronounced in the epigastrium and left hypochondrium, where there was some rigidity. There was an increase in splenic dulness. Rectal examination revealed tenderness over the pelvic peritoneum. He complained during examination that palpation of the abdomen increased his shoulder tip pain. A confident diagnosis of delayed rupture of the spleen was made, and this was confirmed by the abdominal X-ray film, which had been taken in the receiving ward. It showed three of the four classical signs (Figure II).

The patient at first refused operation, insisting that he would recover "without the knife". However, after six hours, during which time the pain had increased, he consented. At operation the abdomen was full of blood and the spleen

FIGURE III.
The spleen removed in Case V.

was found to be lacerated at the hilum and to contain several subcapsular hæmatomata, one of which had burst; the spleen was removed. The pathological report was that the spleen was essentially normal (Figure IV). Convalescence was uneventful.

Spontaneous Rupture of the Spleen.

Sherritt in 1878 reported a case of apparently spontaneous rupture of a normal spleen. Since that time many conflicting opinions have been voiced on this controversial subject.

Roettig *et alii* (1943) refuse to accept that the normal spleen can rupture spontaneously, and tend to attribute reported cases to forgotten minor trauma. It is true that the required trauma is at times very meagre. Black (1933) believes that in the cases of spontaneous rupture reported the spleens had probably undergone premature aging. He avers that many spleens show hyaline changes in their blood vessels early in life. Suffice it to say that the pathological report of the case he published does not support this theory, nor has it found support in any other reports I have seen. Susman (1927) states that spontaneous rupture probably occurs in an area of pathological change in the spleen, that area being completely destroyed by the hæmorrhage. This theory hardly bears critical examination.

Hamilton Bailey (1930), eliminating all chances of forgotten trauma, accepts that spontaneous rupture of a normal spleen must at times occur. Zuckerman and Jacobi (1937) accept it too, and are inclined to attribute the phenomenon to excessive mobility of the spleen.

When one reads the reports of cases published, one must accept that this strange phenomenon in fact does occur.

FIGURE IV.
The spleen removed in Case V.

CASE VI.—F, a housewife, aged fifty-four years, was admitted to hospital on July 21, 1953. Eight hours previously, whilst carrying out her ordinary household duties, she had experienced the sudden onset of gripping upper abdominal pain, particularly in the epigastrium. She became nauseated, but did not vomit. Four hours later she developed acute pain in the back of the neck. Her previous history was not significant. She had had no previous illness, and was the mother of eight children, all born normally. She had never suffered from dyspepsia.

On examination the patient was in obvious pain and was noticed to be moderately pale. Her skin was normal. The blood pressure was 114 millimetres of mercury, systolic, and 60 millimetres, diastolic, and the pulse rate 80 per minute. Tenderness was present across the whole of the upper part of the abdomen, maximal just to the left of the mid-line. Bowel sounds were present. Percussion of the abdomen and lung bases revealed no abnormal dulness. Rectal examination gave normal findings. An X-ray film of the abdomen showed no gas under the diaphragm. Although it was not noticed at the time, the film does show increased opacity in the left upper quadrant and some elevation of the left leaf of the diaphragm. The serum amylase content was 114 Somogyi units.

It was thought that the diagnosis was probably perforation of a peptic ulcer (possibly into the lesser sac), and the abdomen was therefore opened. The abdominal cavity was full of blood, and a ruptured spleen with a large tear running across the hilum was removed. The pathological report was that the spleen was normal in size and showed no evidence of reticulosis, granuloma or neoplasm.

On the twelfth day after operation the patient developed thrombophlebitis in the left lower limb, but this quickly responded to treatment. She was discharged from hospital on August 26.

Direct questioning after the operation failed to reveal the slightest suggestion of trauma to the lower part of the chest or the abdomen at any time.

CASE VII.—G, a labourer, aged fifty-four years, was admitted to hospital on May 10, 1954, because shortly before he had collapsed suddenly at work, with very severe pain under the left costal margin and in the left lower part of the chest. He was in a state of severe shock and was examined by his local doctor, who thought he had had a coronary occlusion. In 1948 he had had a partial gastrectomy for duodenal ulcer. He had been asymptomatic thereafter until six months before his admission to hospital, when he started to experience postprandial epigastric distress, felt particularly to the left of the mid-line. Of late, this pain had been more severe and he had experienced only partial relief with alkalis.

On his admission to hospital his general condition had greatly improved, despite the fact that he was in constant pain. His blood pressure was 145 millimetres of mercury, systolic, and 85 millimetres, diastolic, and his pulse rate was 100 per minute. He was not noticed to be abnormally pale. His chest was clinically clear. The abdomen was tender in all areas, but particularly so under the left costal margin. There was no rigidity. Splenic dulness did not seem to be increased, but it was thought that his abdomen was a little dull in the left flank. On rectal examination, tenderness was present over the pelvic peritoneum, which had a somewhat "boggy" feel. A straight X-ray film of the abdomen showed displacement of the stomach to the right with a crescent-shaped gastric air bubble (see Figure V). It was thought that he probably had a ruptured spleen, and he was submitted to laparotomy. Two or three pints of blood were aspirated from the peritoneal cavity and a severely lacerated spleen was removed (see Figure VI). There was no evidence of anastomotic ulceration.

FIGURE VI.

The spleen removed in Case VII. Note the deep tear in the hilar region and the extensive stripping of the capsule.

The pathological report showed that the spleen was of normal size with a rent across its hilum, and showed no microscopic evidence of abnormality in structure. The patient denied repeatedly that he had been injured in any way prior to his sudden collapse.

Spontaneous rupture of the spleen usually occurs "out of the blue". However, cases have been reported in which the accident was apparently precipitated by a minor strain—for example, lifting a bucket of water, coughing, straining at stool and having a large drink.

Strangely enough, in a significant number of reported cases, people who have sustained spontaneous rupture of a normal spleen have suffered from varying digestive upsets for some time before the accident (Susman, 1927); note the history of postprandial discomfort in Case VII. One wonders whether digestive disturbance can cause excessive hyperæmia and friability of the spleen. There is, of course, no basis at all for this contention.

Treatment.

The treatment of lacerated spleen is surgical. When the diagnosis is made, preparations must be set in hand for early operation. Arrangements are made to start replacing blood lost immediately, and within the limits of reason the principle of "treat shock first" is adhered to. But it must be pointed out that persistence in transfusion in all cases until the blood pressure returns to normal is pure folly. The mortality of operation rises steeply with delay, and once a blood transfusion has been started and the patient has had one or two pints of blood given quickly he should be taken to the operating theatre. Most authorities now emphasize this point (*McIndoe, 1932; Larghero, 1951; Roettig et alii, 1943*). Roettig reports a case in which splenectomy was performed when the blood pressure was 70 millimetres of mercury, systolic, and 40 millimetres, diastolic, and the patient made a good recovery.

Splenectomy is, of course, the only operation to be considered. There is no place these days for tamponade or suture of the spleen. At the conclusion of splenectomy a quick examination of the rest of the abdomen must be made in a search for other injuries. Autotransfusion with the use of the blood recovered from the peritoneal cavity is a tedious and entirely unnecessary procedure these days. Perhaps it might be useful in areas where blood is not freely available.

An immense amount has been written about the technique of splenectomy. The classical paper of recent years is that by Cole (1942). I do not propose to say much on the subject.

Many incisions have been used. Cole prefers a curved left subcostal incision as illustrated in Figure VII.

> The incision starts high up in the epigastrium about 1" to the left of the midline and extends downwards for a distance of two or more inches, then curves rather sharply to the left, being relatively parallel with the costal margin.

The vertical incision opens the anterior rectus sheath. The rectus is retracted laterally, and then the posterior sheath is opened. At the lower limit of the vertical part of the incision the rectus and its sheath are divided transversely. The incision then extends laterally across the oblique and transverse abdominal wall muscles. Cole (1942) holds that this incision gives excellent exposure and divides only one intercostal nerve.

Larghero and Guiria (1951) prefer an abdomino-thoracic incision along the ninth intercostal space—one-third in the thorax and two-thirds in the abdomen. They are delighted with the ease of splenectomy through this incision, and point out that the chest can be opened in a difficult case. Many people prefer a left-sided Kocher's incision. This gives good exposure, but Cole (1942) objects that it divides two, if not three, intercostal nerves and leaves a weakened rectus.

When operating for a ruptured spleen, I think that a long left paramedian or even transrectal incision is best. It gives adequate exposure, is easy and quick to make, and it allows one to make a full examination of the rest of the abdomen. The special incisions discussed above, whilst perhaps ideal for a "cold" splenectomy, have the disadvantage of not allowing an easy examination of all the abdominal contents. Damage to other abdominal viscera is a frequent occurrence, and the incision must give adequate room to discover and repair such lesions. Werbel

et alii (1954) report a case in which a left subcostal incision was used. A ruptured liver as well as a ruptured spleen was found, and the incision proved entirely inadequate to deal with the situation. It had to be extended well across the mid-line and also vertically. Should it

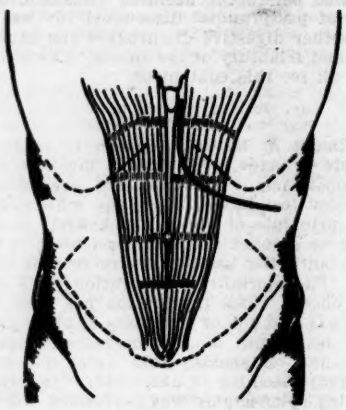


FIGURE VII.
The oblique subcostal incision for splenectomy favoured by Cole (1942). (From *The Surgical Clinics of North America*, February, 1942, W. B. Saunders Company, Philadelphia and London.)

prove difficult to obtain adequate exposure for the delivery of the spleen through a left paramedian incision, then a lateral extension transversely across the rectus can easily be made. (See Figure VIII.)

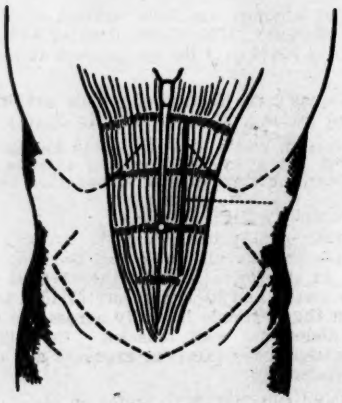


FIGURE VIII.
The long left paramedian incision. The lateral extension which may be necessary is marked by the interrupted line.

With regard to the technique of splenectomy, such refinements as are usually described for the removal of a diseased spleen in a fit patient are probably unnecessary and dangerous. One is not interested in saving any blood which the spleen may hold as a reservoir. Also the spleen is damaged and is often friable, and the pedicle may be severely lacerated. Meticulous dissection of the pedicle in an endeavour to isolate individual vessels for ligation may well be fraught with disaster (note Case III). It is best, first of all, to clamp and divide the gastro-splenic ligament. The spleen can usually then be rotated forwards, the posterior layer of the lieno-renal ligament being divided first if necessary. In a difficult case this division may have to be done blindly by touch rather than under direct vision. Once the spleen is delivered forwards into the wound, the pedicle is clearly visible and can be clamped with safety. It is most unwise to tie the splenic pedicle in one mass ligature. It can be done simply and safely by taking small sections at a time (see Figure IX). In this way a perfectly safe ligature of the pedicle is accomplished, without the necessity of tying individual vessels. One should always clamp the pedicle close to the hilum of the spleen, to avoid the tail of the pancreas.

An alternative method, which has proved very satisfactory in some cases, is to ligate the splenic artery well away from the spleen at the superior border of the pancreas before the spleen has been disturbed at all.

After operation transfusion is continued until blood which has been lost is replaced. A careful watch is kept for the onset of complications, and the appropriate treatment is instituted should they occur.

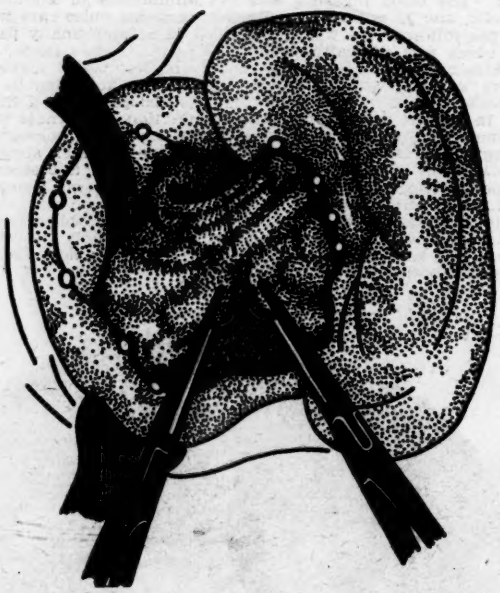


FIGURE IX.
Showing division and ligature of the splenic pedicle in small segments. (Taken from Cole, *The Surgical Clinics of North America*, February, 1942, W. B. Saunders Company, Philadelphia and London.)

The Complications of Splenectomy.

Acute collapse of the lower lobe of the left lung or segments thereof is a very common complication. As soon as signs appear a bronchoscope should be passed and the bronchi aspirated.

Bronchopneumonia is also quite common. It probably is always preceded by collapse of the involved segment of the lung.

Paralytic ileus is one of the commonest sequelæ of splenectomy for traumatic rupture of the spleen (Roettig *et alii*, 1943; McIndoe, 1932; Bailey, 1930; Larghero and Guiria, 1951). Its frequency is due to the original trauma to the abdomen, to blood in the peritoneal cavity and to the trauma of surgery. It is so common that Larghero and Guiria (1951) as a routine procedure aspirated the intestine with an indwelling tube after splenectomy. Certainly, as soon as distension becomes obvious and bowel sounds are few or absent, continuous intestinal decompression should be commenced. Penberthy and Reiners (1953) recommend pre-operative and post-operative aspiration in all cases of abdominal trauma in which operation is undertaken.

Disruption of the wound often occurs after splenectomy and has been reported by practically every writer on the subject. Bailey (1930) reported four out of 32 cases. Probably, as he suggests, it is due to injury to the pancreas, leading to the escape of digestive ferments at the time of operation. Because of the frequency of this complication I think it is wise always to suture the abdominal wall with non-absorbable material, as recommended by Foster and Prey (1940). Of course, this is not the final answer to wound disruption.

Intestinal obstruction from adhesions not uncommonly occurs after splenectomy. Inevitably a large fossa is left after the spleen has been removed, and as this is not completely peritonealized, kinking of the bowel can easily occur. Mechanical obstruction of this type may arise any time after the fifth day. It may, of course, be delayed for years.

The frequency of peripheral thrombophlebitis (Zabinski and Harkins, 1943) is probably contributed to by the great rise in the number of blood platelets in the first two weeks after splenectomy.

Acute dilatation of the stomach may occur before or after operation. It is a complication to guard against in all cases of abdominal trauma (Penberthy and Reiners, 1953; O'Rourke and Cameron, 1953).

Summary.

A review of the pathology, clinical picture and treatment of traumatic rupture of the normal spleen is presented. Attention is drawn to the significant diagnostic features of the condition, and emphasis is placed on the radiological findings which may be present. The analysis of delayed splenic rupture and spontaneous rupture of the normal spleen is made. A short discussion of the technique of splenectomy for ruptured spleen is presented, and the post-operative complications are reviewed. Seven cases are presented, including two of spontaneous rupture and one of delayed rupture with a latent period of eight weeks.

Acknowledgements.

My thanks are due to Mr. W. J. Ferguson, of the West Middlesex Hospital, London, in whose unit most of the patients in the reported cases were treated. I am also most grateful to Mr. C. Osborn and Mr. G. Brosnan, of Saint Vincent's Hospital, Melbourne, for permission to report cases, and to Mr. Brosnan for his generous help in the preparation of this paper.

References.

AIRD, I. (1949), "Companion in Surgical Studies", Livingstone, 826.

BAILEY, H. (1930), "Spontaneous Rupture of the Normal Spleen", *Brit. J. Surg.*, 17: 417.

BLACK, J. M. (1933), "Spontaneous Rupture of the Spleen", *Brit. J. Surg.*, 20: 526.

COLE, W. H. (1942), "The Technique of Splenectomy", *S. Clin. North America*, 22: 43.

COLEMAN, A. H. (1939), "Spontaneous Rupture of the Normal Spleen", *Brit. J. Surg.*, 27: 173.

CONNORS, J. F. (1921), "Ruptured Spleens—Spontaneous and Subcutaneous", *Ann. Surg.*, 74: 1.

FOSTER, J. M., JUNIOR, and PREY, D. (1940), "Rupture of the Spleen—An Analysis of Twenty Cases", *Am. J. Surg.*, 47: 487.

GALVANO, G., and LO GIUDICE, F. (1951), "Late Hæmorrhage following Traumatic Rupture of the Spleen", *Policlinico, sez. prat.*, 58: 1161; abstracted in *Internat. Abstr. Surg.* (1952), 94: 357.

GORDON-TAYLOR, G. (1942), "The Problems of Surgery in Total War, with Special Reference to Abdominal Injuries", *Surg., Gynec. & Obst.*, 74: 375.

GORDON-WATSON, C. (1932), in Choyce, "A System of Surgery", Cassell, 2: 5.

HUESTON, J. T. (1951), "Delayed Splenic Hæmorrhage", *Australian & New Zealand J. Surg.*, 20: 238.

LARGHERO, Y. P., and GUIRIA, F. (1951), "Traumatic Rupture of the Spleen. Statistical Data on Eighteen Cases", *Surg., Gynec. & Obst.*, 92: 385.

LEARMONTH, J. (1951), "Surgery of the Spleen", 2: 67.

MCINDOE, A. H. (1932), "Delayed Hæmorrhage following Traumatic Rupture of the Spleen", *Brit. J. Surg.*, 20: 249.

METCALFE, R. F., and FLETCHER, L. Z. (1922), "Ruptured Spleen, with Report of Three Cases", *Ann. Surg.*, 75: 186.

O'ROURKE, P. V., and CAMERON, D. A. (1953), "Common Injuries to the Thorax", *S. Clin. North America*, 33: 1069.

PENBERTHY, G. C., and REINERS, C. R. (1953), "Nonpenetrating Injuries of the Abdomen", *S. Clin. North America*, 33: 1179.

ROBITTIG, L. C., NUSBAUM, W. D., and CURTIS, G. M. (1943), "Traumatic Rupture of the Spleen", *Am. J. Surg.*, 59: 292.

SKERRITT, E. M. (1878), "Spontaneous Rupture of the Spleen", *Brit. M. J.*, 1: 641.

SUSMAN, M. P. (1927), "Spontaneous Rupture of the Spleen", *Brit. J. Surg.*, 15: 47.

WEBB, R. C. (1940), *Am. J. Surg.*, 47: 497.

WERBEL, E. W., GREENMAN, R., and PETRICK, E. C. (1954), "Complete Rupture of the Left Lobe of the Liver and Spleen with Recovery", *Ann. Surg.*, 139: 112.

WRIGHT, L. T., and PRIGOT, A. (1939), "Traumatic Subcutaneous Rupture of the Normal Spleen", *Arch. Surg.*, 39: 551.

ZABINSKI, E. J., and HARKINS, H. N. (1943), "Delayed Splenic Rupture: A Clinical Syndrome following Trauma", *Arch. Surg.*, 46: 186.

ZUCKERMAN, I. C., and JACOBI, M. (1937), "Spontaneous Rupture of the Normal Spleen", *Arch. Surg.*, 34: 917.

Legends to Illustrations.

FIGURE II.—Straight X-ray film of the abdomen in Case V, showing: (*a*) displacement of the stomach to the right with a crescent-shaped gastric air bubble; (*b*) increased opacity in the left upper quadrant of the abdomen; (*c*) elevation of the left half of the diaphragm.

FIGURE V.—Straight X-ray film of the abdomen in Case VII, showing displacement of the stomach to the right, with a crescent-shaped gastric air bubble.

Reports of Cases.

CARDIO-ŒSOPHAGEAL INTUSSUSCEPTION AND OPERATIVE CURE.

By KENNETH W. STARR,
Sydney.

A FEMALE patient, now aged fifty-two years, had her first pregnancy in 1928. After parturition she noticed that the contents of her stomach regurgitated in large quantities whenever she "bent over". This state of affairs continued until 1948, when after an appendicectomy regurgitation would occur without her bending over. She always felt better after emptying her stomach. Epigastric and substernal pain had begun six months previously; it was severe, aggravated by food, relieved by alkalis and "Banthine" and liable to spontaneous remission for about three or four weeks at a time. During the previous three months she had lost 14 pounds in weight, and it was on this account that she sought medical advice.

No abnormality was detected on physical examination of the patient except high epigastric tenderness. A fasting test meal examination revealed hyperchlorhydria. X-ray examination with a barium meal (Figure I) was reported upon by Dr. F. N. Rodda as follows:

> The opaque meal passed freely and rapidly down a very wide œsophagus into the stomach and there was no sign of œsophageal irregularity. The stomach was seen to be regular and of normal tone, and there was no evidence of gastric malignancy or ulcer or of duodenal ulceration. With the patient lying supine and the head slightly lowered there was a marked reflux of the opaque meal into a wide œsophagus which appeared to be quite atonic, but neither in this nor in a lateral projection was there any sign of hiatus hernia. The impression gained was of complete incompetence of the cardio-œsophageal sphincter. In the three films taken with the patient lying prone there was a peculiar ring-like conformation shown by the opaque meal at the cardiac end of the stomach for which I am unable to account.

My opinion was sought lest a cardiac carcinoma should be present; but I could find no evidence of this condition and considered that the picture with the patient in the prone position was diagnostic of the intussuscepted state.

Operation was advised and undertaken through the left seventh rib bed. The œsophageal orifice of the diaphragm admitted four fingers and the cardio-œsophageal intussusception was rapidly produced and reduced. Repair by the crura was first carried out, and the œsophageal orifice itself was reinforced by a tendinous flap cut from the outer aspect of the orifice to surround the œsophagus (Figure II).

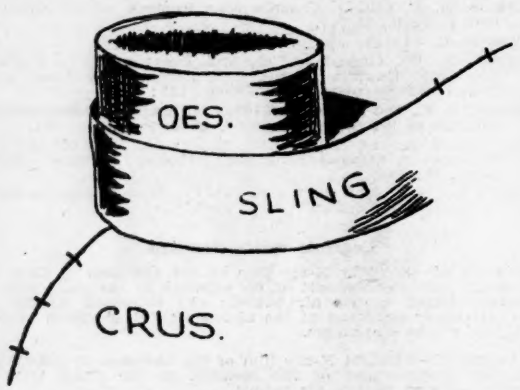


FIGURE II.
Operative plan: (i) Allison's procedure for hiatus hernia; (ii) diaphragmatic fascial sling.

The patient had an uneventful convalescence. Her diet had to be restricted to soft foods for three months after operation because of the sense of lower œsophageal obstruction. However, since then she has been symptomless and eats at will.

Comment.

The condition is said to be very rare, but the symptoms and distinctive barium meal findings should render its recognition easy. The operative procedure described presents no difficulties.

References.

FELDMAN, M. (1948), "Clinical Roentgenology of the Digestive Tract", Third Edition, Williams and Wilkins, Baltimore, 286.

LIARIS, G., and RICARD, E. (1934), *"Dilatation circonférentielle de l'œsophage médiastinal par invagination partielle gastro-œsophagienne", Ann. d'anat. path.*, 11: 868.

Legends to Illustrations.

FIGURE I.—The "barium ring" in the intussuscepted œsophagus presents a distinctive picture.

FIGURE III.—The dilated œsophagus has not returned to normal after operation.

ASPIRATION BIOPSY OF THE KIDNEY IN THE APPRAISAL OF UNILATERAL RENAL DISEASE WITH HYPERTENSION: REPORT OF A CASE.

By BRIAN L. MARKS,
Chief Registrar, The Royal Melbourne Hospital, Melbourne.

RECENTLY great interest has been displayed in the treatment of hypertension. However, most of such treatment is symptomatic, and for this reason hypertension associated with unilateral renal disease has attracted more attention than the number of reported cures would seem to merit. None the less, this approach is fully justified, both by its influence upon our understanding of hypertension in general and by an occasional spectacular result.

One disappointment of these cases has been the failure to relieve some patients who have no apparent involvement of the remaining kidney by the primary pathological process. Further study of such patients is clearly needed in order to determine the reasons for this failure.

In the case to be described, in which great relief has been obtained to date, needle biopsy of the "normal" kidney was employed prior to removal of the opposite kidney.

Clinical Record.

A housewife, aged twenty-four years, was admitted to the Royal Melbourne Hospital on October 6, 1953, for investigation of hypertension. Her past history revealed frequent attacks of tonsillitis as a child with no known sequelæ, culminating in tonsillectomy at the age of twelve years. At five years she suffered an uncomplicated attack of scarlet fever. In addition, she had been troubled by bronchial asthma for some years. There was no family history of hypertensive, cardio-vascular or renal disease. In her first pregnancy, four years before her admission to hospital, she had remained well, her urine was always free of albumin and her blood pressure was persistently within normal limits. No history of "pyelitis" could be obtained. She was delivered at term of a healthy baby. Her second pregnancy two years later followed the same pattern throughout.

She was again examined at the Royal Women's Hospital, Melbourne, on April 28, 1953, when pregnant for the third time, fifteen weeks having passed since her last menstrual period. Examination of the patient then revealed no abnormality, although her blood pressure was 150 millimetres of mercury, systolic, and 100 millimetres, diastolic.

At twenty-one weeks her blood pressure was 150 millimetres of mercury, systolic, and 105 millimetres, diastolic, but there was no albuminuria. At this time she developed frequency of micturition without scalding, which persisted until operation, and became such that she passed urine six times by day and six times by night. She was admitted to hospital for assessment, during which period her systolic blood pressure remained at 140 millimetres of mercury and her diastolic blood pressure varied between 80 and 90 millimetres of mercury. Her urine was repeatedly free of albumin. X-ray examination of her chest and a full blood examination gave normal results.

When she was twenty-four weeks pregnant, her blood pressure was 140 millimetres of mercury, systolic, and 90 millimetres, diastolic, but her urine contained "one-sixteenth" albumin. She said that she had felt no recent movements and the fœtal heart was inaudible. She was readmitted to hospital for one week, when the proteinuria cleared. Microscopic examination of her urine gave normal results and her blood pressure was normal.

At twenty-six weeks her blood pressure and urine were normal. Her hæmoglobin value was 10·7 grammes per 100 millilitres, and she began an intravenous course of iron therapy. Her second injection was administered one week later without immediate incident. Three days later she developed an allergic reaction to the iron, which responded rapidly to adrenaline.

Her final ante-partum admission to hospital, on August 3, when she was twenty-eight weeks pregnant, was necessitated by complaints of nausea, headache and vomiting of two days' duration, associated with a blood pressure of 170 millimetres of mercury, systolic, and 120 millimetres, diastolic, mild dependent œdema and slight albuminuria. During the next few days this state persisted despite sedation. Her blood urea content was 23 milligrammes per 100 millilitres, and microscopic examination of the urine revealed no abnormality.

The oral administration of "Vegolysen" was then commenced, but despite its trial in increasing dosage over a period of two weeks, her blood pressure ranged as high as 170 millimetres of mercury, systolic, and 130 millimetres, diastolic. Her urine remained free of protein. When she received heavy sedation instead of "Vegolysen", further œdema developed. Under treatment with hexamethonium bromide by hypodermic injection she became free of

œdema, and her blood pressure settled to 160 millimetres of mercury, systolic, and 100 millimetres, diastolic.

Three days later, when a small ante-partum hæmorrhage occurred, artificial rupture of the membranes was undertaken. Despite intensive medical stimulation she did not come into labour; however, her condition remained good.

After one week an intravenous infusion of "Pitocin" was commenced, and she came promptly into labour, being delivered on September 2 of a boy weighing three and a half pounds. The baby has since thrived. That evening she was well, apart from her blood pressure, which was 190 millimetres of mercury, systolic, and 140 millimetres, diastolic. *Post partum*, her urine contained little albumin, but her blood pressure was persistently raised. It was decided to discontinue hexamethonium therapy, and this step did not materially affect her condition.

On the seventh day after delivery she developed fever and loin pain with tenderness in the left renal angle. Culture of her urine yielded *Escherichia coli*. Treatment with streptomycin proved effective; but she left hospital against advice on the ninth day *post partum*, when she was still pyrexial.

She was next examined twenty-seven days after delivery, when she was comatose, cyanosed and having frequent convulsive seizures. This process had started the preceding evening with the complaint of severe headache. Her blood pressure was 170 millimetres of mercury, systolic, and 150 millimetres, diastolic. Retinoscopic examination revealed bilateral papilloedema, together with the presence of a small exudate in the right fundus. Her urine repeatedly boiled solid with albumin. The blood urea content was 32 milligrammes per 100 millilitres.

"Hydergine" was administered by continuous intravenous infusion without effect, so that the administration of "Vegolysen" by injection was once more commenced. After one week, during which time her conscious state improved, the hypertension and albuminuria gradually decreased in severity.

She was transferred to the Royal Melbourne Hospital on October 6.

Initial examination disclosed her to be a thin but otherwise apparently healthy young woman. Her blood pressure was 180 millimetres of mercury, systolic, and 110 millimetres, diastolic, and there were slight cardiac enlargement and some tenderness under the right costal margin. Her retinal arteries were slightly thickened, and an old exudate was present in the right fundus. The urine was free from abnormality, both chemically and mircoscopically.

The administration of "Vegolysen" was continued by injection, but even so her blood pressure varied from 150 to 190 millimetres of mercury, systolic, and from 110 to 120 millimetres, diastolic. Renal function tests revealed a blood urea content of 40 milligrammes per 100 millilitres, a maximum urea concentration of 2%, and a total excretion in three hours of five grammes.

It was decided to perform a renal biopsy, in order to attempt to exclude a late puerperal eclampsia. As is usual, this was preceded by intravenous pyelography (Joske, 1954), and this examination produced a normal pyelogram with good excretion on the right, but no dye shadow on the left even after forty minutes.

Right renal biopsy was uneventful. Microscopic examination of sections of the tissue (Figures I and II) showed five glomeruli. There were a few areas of capillary basement membrane thickening, but the capillaries were patent and not excessively cellular. In the juxtaglomerular arterioles no significant thickening was detected, but a larger arteriole had a slightly hypertrophied wall. No arteries were included in the material. There was no interstitial fibrosis or cellularity, but the tubules appeared slightly dilated, and some convoluted tubules contained protein material; others contained blood. The anatomical changes appeared minimal, and the tubular dilatation may have been related to a work hypertrophy.

Subsequently, a left retrograde pyelographic examination was performed, and revealed a normal pelvi-calyceal system in a kidney somewhat smaller than that on the right. No specimen of urine was collected from the catheter.

FIGURE III.
Cut surface of left kidney.

Left renal biopsy was attempted, in order to determine the nature of the pathological process, but no renal tissue was obtained. The procedure was not repeated.

A normal electrocardiogram was obtained, but an Addis count disclosed excessive pus cells in the urine. Intravenous pyelography was repeated, and the findings were unchanged.

Left nephrectomy was decided upon, and was performed on November 10. The kidney (Figure III) was nine centimetres long and 3·5 centimetres thick. Its surface was injected and finely granular. On section the cortex was pale and about six millimetres wide. It was regular and well demarcated from the medulla.

On microscopic examination (Figures IV and V) most of the glomeruli showed thickening of Bowman's capsule, and there was some adhesion of the tufts in many glomeruli, but gross fibrosis was not present. Some of the tubules were dilated and contained casts, many groups of round cells were present between them, and there was some fibrosis. Arterioles were not prominent, but medium vessels were thickened. The changes were those of chronic pyelonephritis, probably of some months' duration.

Post-operatively the patient developed an acute urinary tract infection, the causative organism again being *E. coli*. Vomiting was considerable, and oliguria and hypotension were severe. She was treated with fluid and electrolyte replacement, antibiotics, and "Neosynephrin", when her blood pressure rose and the urinary output improved. One week after operation, microscopic examination of her urine gave normal findings, and the serum electrolyte and blood urea levels were normal. On her discharge from hospital, on the tenth day after operation, her blood pressure was 150 millimetres of mercury, systolic, and 90 millimetres, diastolic, and her urine was clear.

Subsequently, she has been followed as an out-patient for a period of ten months. Over this time (Figure VI) her blood pressure has fallen progressively, and is now 110 millimetres of mercury, systolic, and 80 millimetres, diastolic. Her heart is now of normal size, and retinoscopic

examination reveals no abnormality. The blood urea levels and the findings on microscopic examination of the urine have been normal repeatedly. Renal function tests show a total urea excretion of 5·3 grammes in three hours with a maximum concentration of 2·3%.

The patient feels well apart from pain under her nephrectomy scar, and can perform a hard day's work without undue fatigue. Occasionally she passes urine at night, but never more than once.

Comment.

Many cases such as this have been described previously. Whilst cure seems likely, it is not established, as more prolonged follow-up may show.

It may be presumed, in retrospect, that the pyelonephritis was unilateral, as the patient's urine has been normal since operation (Pickering and Heptinstall, 1953).

A feature of the case deserving further comment is the biopsy of the unaffected kidney prior to nephrectomy, so that it is perhaps justifiable to discuss the possible value of the procedure in this condition.

Discussion.

The following factors are those of greatest importance in determining the prognosis in an individual case.

1. The hypertension not being due to renal disease. This is more likely when there is a family history of hypertension (Platt, 1948*a*). It has been suggested that such familial hypertension may be caused to appear earlier than it otherwise would by renal ischæmia (Braasch, 1952). Such patients may perhaps show a late rise in blood pressure after nephrectomy, but no figures relating to this topic have yet appeared.

2. The involvement of both kidneys by the primary pathological process (Pickering and Heptinstall, 1953).

3. The occurrence of contralateral renal ischæmia from vascular changes consequent upon the presence of hypertension (Sensenbach, 1944). This is said to be more likely in patients aged over fifty years (Braasch, 1952; Sensenbach, 1944), perhaps in those with long-standing hypertension, and possibly in malignant hypertension (Pickering and Heptinstall, 1953). However, improvement may occur despite bilateral vascular changes (Pickering and Heptinstall, 1953). Crabtree and Chaset (1940) consider that such vascular damage is of no importance in prognosis, but most disagree with their view (Braasch, 1952; Platt, 1948; Sensenbach, 1944; Wilson, 1945 and 1952).

Against this background, renal biopsy may be considered as a pre-operative investigation, especially with a view to the patient's suitability for nephrectomy. The procedure is safe (Iverson and Brun, 1951), but special care is necessary here as the biopsy must be taken from the better kidney. Left renal biopsy carries greater risk than right, and cannot in general be recommended, so that the procedure is virtually limited to left renal disease with hypertension.

Biopsy would need to be of more assistance than individual renal function tests performed by ureteric catheterization. This latter procedure has not proved entirely satisfactory in all hands, but the comparative value of the two procedures remains to be assessed.

Any change present on the "normal" side is unlikely to be gross, as, if it were, total renal function would probably be reduced, so that operation would not be considered.

In theory, renal biopsy could be used to reveal whether pyelonephritis was truly unilateral. However, the specimen of tissue obtained by needle biopsy is small (average about nine glomeruli) and is not necessarily representative, especially in a condition such as chronic pyelonephritis. In this latter, even when it is advanced, there may be present areas of normal renal tissue (Longcope and Winkenwerder, 1933; Pickering and Heptinstall, 1953). As the process is necessarily not advanced, such areas are even more likely.

The value of the investigation in determining the presence and degree of sequential vascular changes is yet to be explored. Some say that such changes are not patchy (Weiss and Parker, 1939). However, by analogy from the experiments of Wilson and Byrom (1939) the changes may well be patchy, especially in the early stages.

From this point of view the procedure shows some promise. If vascular lesions are found to be pronounced, then operation is probably inadvisable (Wilson and Byrom, 1941).

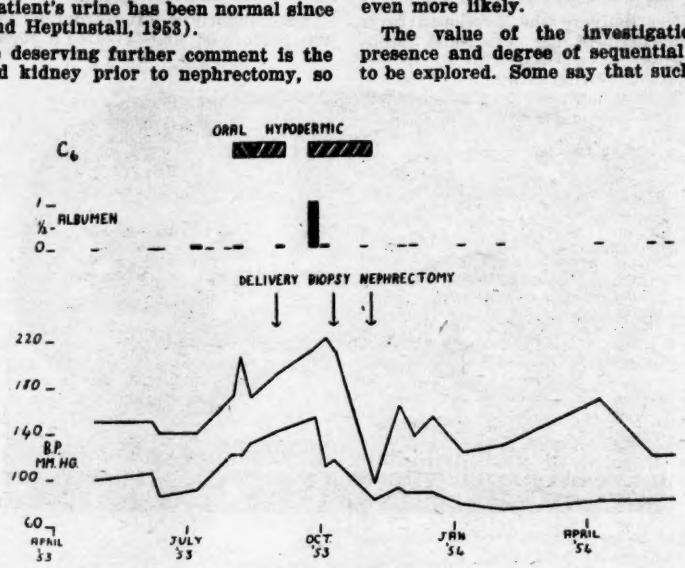


FIGURE VI.
Chart of patient's course up to seven months after nephrectomy.

Conclusion.

Renal biopsy may be of assistance in deciding against nephrectomy. This is important, in so far as useless nephrectomy may accelerate the course (Pickering and Heptinstall, 1953; Wilson, 1952), and thereby prohibit effective symptomatic treatment.

Should normal renal tissue be obtained, and other indications be favourable, then nephrectomy must be performed. This circumstance, however, should not be taken to imply a good ultimate prognosis.

Pre-operative right renal biopsy, when the left kidney is obviously diseased, may perhaps be considered, especially indicated in those cases in which, despite the presence of an apparently unilateral lesion, other indications are less favourable or definite, such as the following: (i) age over fifty years; (ii) hypertension of long standing (over two years); (iii) the presence of severe or malignant hypertension (perhaps); (iv) when the "normal" kidney does not show compensatory enlargement (Braasch, 1952); (v) when the diseased kidney is not functionless (Sensenbach, 1944; Langley and Platt, 1948); (vi) when a family history of hypertension is present; (vii) possibly when there is no indication for operation other than hypertension (Hardwick and Badenoch, 1947).

Summary.

A case is presented in which nephrectomy was performed for unilateral chronic pyelonephritis with hypertension.

Aspiration biopsy of the unaffected kidney was performed prior to nephrectomy.

The possible value of this procedure in such cases is discussed.

Acknowledgements.

I am indebted to Dr. W. McI. Rose for permission to publish this case and for his help; to Dr. J. L. Frew and Dr. R. A. Joske for advice on preparation of this report; and to Dr. J. D. Hicks and Mr. R. Inglis for their assistance with photographs.

References.

BRAASCH, W. F. (1942), "Surgical Kidney as an Ætiological Factor in Hypertension", *Canad. M. A. J.*, 46 : 9.

BRAASCH, W. F. (1952), "End Results Following Nephrectomy in Patients with Hypertension", *J. Urol.*, 68 : 6.

BRAASCH, W. F., WALTERS, W., and HAMMER, H. (1940), "Hypertension and Surgical Kidney", *J.A.M.A.*, 115 : 1837.

CASTLEMAN, B., and SMITHWICK, R. (1943), "Relation of Vascular Disease to Hypertensive State Based on Study of Renal Biopsies from 100 Hypersensitive Patients", *J.A.M.A.*, 121 : 1256.

CRABTREE, E., and CHASET, W. (1940), "Vascular Nephritis and Hypertension; Combined Clinical and Clinicopathologic Study of 150 Nephrectomized Patients", *J.A.M.A.*, 115 : 1842.

HARDWICK, C., and BADENOCH, A. W. (1947), "Place of Unilateral Renal Disease in Hypertension", *Brit. M. J.*, 1 : 293.

IVERSON, P., and BRUN, C. (1951), "Aspiration Biopsy of Kidney", *Am. J. Med.*, 11 : 324.

JOSKE, R. A. (1954), "A Technique for Aspiration Biopsy of the Kidney", *Australian Ann. Med.*, 3 : 44.

LANGLEY, G., and PLATT, R. (1947), "Hypertension and Unilateral Renal Disease", *Quart. J. Med.*, 16 : 143.

LONGCOPE, W., and WINKENWERDER, W. (1933), "Clinical Features of Contracted Kidney Due to Pyelonephritis", *Bull. Johns Hopkins Hosp.*, 53 : 255.

MATHISEN, H. S. (1951), "Arterial Hypertension in Unilateral Renal Disease with Inhibition of Growth, Treated with Nephrectomy", *Acta med. scandinav.*, 139 : 421.

PICKERING, G., and HEPTINSTALL, R. (1953), "Nephrectomy and Other Treatment for Hypertension in Pyelonephritis", *Quart. J. Med.*, 22 : 1.

PLATT, R. (1947), "Heredity in Hypertension", *Quart. J. Med.*, 16 : 111.

PLATT, R. (1948), "Severe Hypertension in Young Persons; Study of 50 Cases", *Quart. J. Med.*, 17 : 83.

SENSENBACH, W. (1944), "Effects of Unilateral Nephrectomy in Treatment of Hypertension; Evaluation", *Arch. Int. Med.*, 73 : 123.

WEISS, S., and PARKER, F. (1939), "Pyelonephritis; Its Relation to Vascular Lesions and to Arterial Hypertension", *Medicine*, 18 : 221.

WILSON, C. (1945), "Experimental Hypertension and Bright's Disease", *Proc. Roy. Soc. Med.*, 39 : 61.

WILSON, C. (1952), "Experimental Hypertension; Clinical Significance of Animal Studies", *Brit. M. Bull.*, 8 : 316.

WILSON, C., and BYROM, F. B. (1939), "Renal Changes in Malignant Hypertension; Experimental Evidence", *Lancet*, 1 : 136.

WILSON, C., and BYROM, F. B. (1941), "Vicious Circle in Chronic Bright's Disease. Experimental Evidence from Hypertensive Rat", *Quart. J. Med.*, 10 : 65.

Reviews.

Illustrated Handbook of Child Care from Birth to Six Years. Compiled and illustrated by Wava McCullough, assisted by Marcella Gawronski, R.N.; 1954. New York: McGraw-Hill Book Company, Incorporated. 9½" × 6¼", pp. 240, with about 400 illustrations. Price: $4.00.

ANY book recommended by Arthur Parmelee deserves at least passing notice, but the "Illustrated Handbook of Child Care from Birth to Six Years" by Wava McCullough is one four dollars' worth that the average Australian parent need not trouble to read. The only excuse a writer has for adding to the confusing collection of books available on child care is that the material is presented in a new way and is up to date. This writer has that excuse. The book depends on numerous drawings, about four to a page, to illustrate its points, with the text beside them. This is an excellent method, but to succeed the drawings must be good and the text clear; in this case, though there are many attractive drawings, they are on the whole amateurish and the text is printed in a rather irritating type, a mixture of handwriting and handwritten printing. Also when the pictorial method is used so extensively it is essential that the drawings should contain no inaccuracies. On the whole they are accurate apart from their anatomical deficiencies, but most doctors will regard with horror the baby being held forcibly on its back while vitamin concentrate is administered by pipette and will wonder if the incidence of lipoid pneumonia will rise in the United States of America. The posture for artificial feeding is unsatisfactory, and one can only regard with some surprise the sleeping infant clutching his half-consumed bottle of milk. Has the *laissez-faire* method of child care so swept America that the baby now takes its bottle to bed, feeds itself and has a snack when it awakes?

The author as far as one can ascertain is a nurse or health educator more interested in educational methods than in babies, and the real trouble with the book seems to arise from the fact that she and her assistant have not always the clear basic knowledge necessary to write a book such as this. If they had, such statements as the following could not appear: when breast feeding "lean forward to allow milk to flow toward the nipple". The author also recommends weaning at four to five months. The "Do what your doctor says" tone about the whole book with no adequate reasons is no longer acceptable to Australian parents who appear to prefer an authoritative book by a doctor who can combine common sense with explanations and reasons. The subject matter includes child development, play, travelling with baby, the duties of a sitter, nursing sick children and first aid, and in all cases the less medical sections are better done and at times reach a high standard. However, the time has come to protect Australian parents from unnecessary literature. This book must be classed under this category; it has many faults and all its good advice is at present available in cheaper and better books.

The Care of Children: From One to Five. By John Gibbens, M.B. (Cambridge), M.R.C.P. (London); Fifth Edition; 1954. London: J. and A. Churchill, Limited. 7½" × 5", pp. 214, with 10 illustrations. Price: 5s.

"THE CARE OF CHILDREN: FROM ONE TO FIVE", by Dr. John Gibbens, has been a popular handbook for British parents for nearly twenty years and deservedly so, but this fifth edition has to some extent failed to keep abreast of modern child care, and though it is full of common sense, it is marred by occasional inaccuracies.

The subject matter covers all aspects of child care from infant feeding and nursing the sick child to suitable books and toys and behaviour problems. The style is attractive, and simple vivid language is addressed directly to the parent, so that the parent may well visualize a fatherly doctor who loves children and knows them well. However, this very method of approaching parents makes it essential that the information should be reliable, and one must feel uneasy at parents reading such statements as that overweight can cause eczema and convulsions; also it is surprising that a man who can write such a sympathetic understanding chapter on childhood fear can also recommend that a child should be allowed to cry himself to sleep in the process of "getting him trained". It must also be very depressing to the city mother to read that tinned baby foods are undesirable; in fact the whole chapter on feeding savours just a little of the crank. There is no pedantic child psychology or technical terminology in this book and all parents will appreciate its common sense and learn much from it. It is a pity that it is necessary to add that doctors recommending it to their patients should be aware of its limitations.

Text-Book of Ophthalmology. By Stewart Duke-Elder, K.C.V.O., M.A., LL.D., D.Sc. (St. And.), Ph.D. (London), M.D., F.R.C.S., Hon. D.Sc. (Northwestern), M.D. (Dublin), D.M. (Utrecht, Strasbourg), F.R.C.S. (Edinburgh), F.A.C.S.; 1954. Volume VI: Injuries. London: Henry Kimpton. 10" × 7", pp. 1224, with 1145 illustrations, 144 in colour. Price: 105s.

THE 1195 pages of the sixth volume of Sir Stewart Duke-Elder's "Text-Book of Ophthalmology" are given over to the description of injuries to the eye, the majority of which occur in industry.

Like the preceding volumes, this copiously illustrated compendium will long remain an authoritative source of reference. Nevertheless, it is a melancholy fact that if the simple precepts given in the few pages on the prevention of injuries to the eye were adhered to, most of the remainder of the volume could be discarded. Ramazzini, the "Father of Industrial Medicine", realized early in the eighteenth century that the "main difficulty lay in the impossibility of persuading the workers to take the simplest precautions to protect themselves". The outlook of the worker remains unchanged and too many eyes are still being lost in routine industrial procedures because of the lack of the simplest precautions. No operation in surgery is more dramatic than the successful removal of a foreign body from the posterior

segment of the globe by the giant magnet. Unfortunately the elation of the surgeon is rapidly chilled by the reflection that 60% of such eyes eventually retain no useful vision. This places the simple act of using a hammer in the list of dangerous occupations—a position which no worker with "common sense" will accept. Until he does accept it he will remain constantly exposed to the risk of an accident which may seriously reduce or eliminate his capacity as a breadwinner.

The light-hearted attitude of the worker to the hazards of his occupation is a challenge to the industrial medical officer. It must be broken down before any scheme for the prevention of injuries to the eye can succeed.

This sixth volume of Duke-Elder's "Text-Book of Ophthalmology", which should be in the library of every practitioner of industrial medicine, indicates all too vividly the necessity for such a scheme.

Ancient Therapeutic Arts: The Fitzpatrick Lectures Delivered in 1950 and 1951 at the Royal College of Physicians. By William Brockbank, M.A., M.D. (Cambridge), F.R.C.P.; 1954. London: William Heinemann (Medical Books), Limited. 10" x 6¾", pp. 162, with 88 illustrations. Price: 25s.

FEW medical historians seem to have had the incentive to probe deeply into the origins and techniques of ancient therapeutic procedures. Nevertheless, these procedures represent an earnest attempt on the part of an imaginative medical profession to relieve credulous patients from anxiety and bodily discomfort when afflicted with some intractable disease. Many of the methods employed appear crude, irrational, and even dangerous to the life of a patient. Hence, a real historical interest in these weird forms of treatment has been lacking, and the details relating to their application are not well understood.

Medical historians, therefore, will be grateful to Dr. William Brockbank for devoting his Fitzpatrick Lectures (1950-1951) at the Royal College of Physicians to a painstaking investigation of this rather obscure sidelight to medical practice of earlier times. The value of these essays is considerably enhanced by a unique method of presentation; the text is profusely illustrated by rare woodcuts and prints which clearly demonstrate the kind of apparatus used, and show the methods actually being put into practice by doctor or patient.

The subject is divided into four sections treating fully yet succinctly with the ancient arts of enema administration, cupping and leeching, and counter-irritation; while the last chapter gives an exhaustive and interesting account of the less ancient art of intravenous injection of drugs. It may be an open confession of ignorance to admit surprise on learning that the antiquated Chinese practice of moxibustion had been used occasionally in Europe until the early nineteenth century.

All the illustrations are usefully and artistically displayed. Unfortunately there is no index, but a full bibliography is provided at the end of each chapter.

Notes on Books, Current Journals and New Appliances.

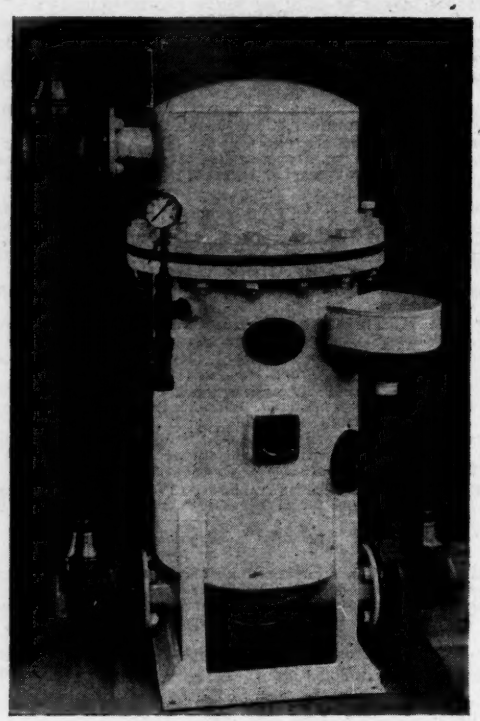
THE "STELLAR FILTER".

THE "Stellar Filter" of the Paterson Engineering Company, Limited, of Windsor House, Kingsway, London, has been specially developed for medical and laboratory use where a very fine filtration is required.

It is extensively employed, for example, in the production of fine chemicals, insulin, liver and similar animal extracts and other injection solutions, all of which must, of course, be completely free from any suspended matter.

The filter consists essentially of a cylindrical shell and outlet manifold constructed to take Stellar patented wire-wound elements or candles, which are fine strainers and are employed as the foundation for a deposited filter bed of filtering powder, known as "Stellafilt", which may be kieselguhr graded for the particular purpose, or an admixture of kieselguhr with other materials.

The element consists of a tube with equally spaced longitudinal ribs having a screw thread cut along the entire length, providing on each rib a series of grooves in which the consecutive turns of wire wound on the ribs are firmly located. The openings over the whole area of the element are of regular size; the result is a rigid element with the shortest possible flow and the minimum gap, and the regularity of the openings ensures an even coating of filter aid with no break which would permit unfiltered liquid to by-pass, thus ensuring absolutely uniform filtration.



As regards materials of construction, filter shells for general purposes with aqueous liquids are made of mild steel and lined when necessary with a hard plastic enamel. For foodstuffs and corrosive conditions stainless steel is used. The filter elements for water, oils and non-corrosive liquids are made with extruded brass tubular cores, electro-tinned and wound with either "Monel" or stainless steel wire. Where it is imperative that the residual liquid should be conserved, special arrangements can be offered according to the nature of the application—siphon type elements, a reversible filter on trunnions or a separate small filter for dealing with the contents of the main filter.

The filtration of liquids containing other than a small amount of suspended matter is usually facilitated by the use of filter aid as a continuous addition throughout filtration. This addition of filter aid inhibits the formation of a skin of dirt on the pre-coat, and by the deposition of further porous material continuously maintains an open filter bed throughout the run. The "Stellar Jet Filtraider" enables this filter aid to be introduced proportionately into the stream of liquid immediately before the filter, and the abrasive diatomite does not pass through the pump.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Clinical Aspects of the Autonomic Nervous System", by L. A. Gillilan, Ph.D., M.D.; 1955. London: J. and A. Churchill, Limited. 8½" x 6", pp. 328, with 42 illustrations. Price: 45s.

The book is in two parts. The first is purely anatomical; the second deals with innervation of organs and systems and with some clinical applications.

The Medical Journal of Australia

SATURDAY, MAY 7, 1955.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words of phrases.

References to articles and books should be carefully checked. In a reference the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those adopted by the Quarterly Cumulative Index Medicus. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

THE EVALUATION OF REMEDIES.

THE steady stream of new and potent drugs pouring out from the manufacturers' laboratories and the avidity of the general public, spurred on by the popular Press, for new therapeutic wonders make a critical attitude on the part of the practising doctor more than ever important today. More valuable still is the clinical assessment of a new drug by some responsible authority before the drug appears on the general market. In this field, particularly valuable work has been done through clinical trials organized by the Medical Research Council in Great Britain both prior to the second World War through the Therapeutic Trials Committee and subsequently through a series of special trials committees. This work has been described from first-hand experience by F. H. K. Green.[1] His paper has a particularly interesting introduction in the form of an historical survey of methods used in the past to evaluate drugs and other schemes of treatment. For convenience, Green subdivides the general methods used into observation, authority and experiment, although he agrees that these methods often overlap. He points out that apart from the experimental factor inherent in all therapy, there is abundant evidence from the history of medicine and pharmacy that the experiential or empirical method (that is, the method of observation) is the oldest way of assessing remedies; and it has given us many active drugs that have been used for centuries and are still used today. It can still make significant contributions to medical progress, but there are serious drawbacks in accepting it as a final means of assessing the value of a drug. Among the agents that it has been responsible for bringing into permanent use are castor oil, opium, squill, and sulphur and mercury used locally for skin diseases, with the possible addition of quinine, digitalis, ergot, the salicylates, caffeine and emetine. Thus, despite the scientific shortcomings of the empirical method, it needs to be remembered that, as Green puts it, a remedy is not necessarily bad just because it is old and has been evaluated by common experience rather than by critical trial. He finds little in favour of authority alone as a criterion of value in therapeutics. It has contributed largely to the continuity of medical and pharmaceutical learning, but that learning has often been unsound and even fantastic. This has meant that the weight of authority has perpetuated useless agents at the expense of developing sound ideas. Green states that the voice of authority is still present today to complicate our assessment of remedies, taking the form of the Press conference, of premature newspaper publicity and of advertisements of the testimonial type. The method of experiment is, of course, the one that has been accepted in modern times. Green quotes many interesting examples of the use of this method, but it appears not to have come into any general use before the eighteenth century. Four notable examples of that time are mentioned: the (fortunately) successful experiments in smallpox inoculation carried out to the orders of Queen Caroline on Newgate prisoners and "charity children" before she would allow the royal children to be inoculated, Jenner's trials of vaccination with cowpox, William Withering's ten-year study of the foxglove as a remedy for cardiac dropsy, and James Lind's controlled trial of the value of oranges and lemons in curing scurvy in sailors at sea.

The work of the Therapeutic Trials Committee of the Medical Research Council was begun in 1931 in response to a request by the Association of British Chemical Manufacturers for an authoritative body to arrange clinical tests of new remedies which in laboratory experiment had given promise both of therapeutic value and of low toxicity. The conditions governing the committee's work were agreed between the Council and the Association, and have formed the basis on which the Council has considered applications for clinical trials ever since. The most important are, first, that the nature and composition of the remedy must be disclosed by the applicant, and second, that the Council reserves the right to authorize publication of the results, whatever their nature, if they believe publication to be in the interests of the medical profession and the public. Among important drugs successfully launched into practical medicine by reports to the Therapeutic Trials Committee were calciferol, "Prontosil", sulphanilamide and stilbœstrol. In this work, especially when control patients were included, it was early realized that the medical statistician was a valuable member of the planning team. As Green neatly puts it, "his role in regard to the investigation should be that of obstetrician, rather than morbid anatomist, for it is unfair to expect him to extract scientific knowledge by performing a kind of mathematical post mortem upon the numerical remains of a badly planned study". The relationship of the statistician to his clinical colleagues is of great importance, and it is pointed out that this must be a scientific partnership and never in any circumstances a dictatorship by one party against the other's wishes. Best of all is for the clinician himself to acquire the skills

[1] *Lancet*, November 27, 1954.

that the statistician is willing to impart, so that the roles of the two experts may be combined in one individual. Green goes on to refer to the fact that during the war, the Therapeutic Trials Committee, which had become of unwieldy size, was allowed to lapse and the Medical Research Council appointed instead special committees to organize tests of particular remedies or methods of treatment. The most active of these was the Penicillin Clinical Trials Committee. After the war, this policy of appointing special committees to cover particular parts of the field was continued, and important work has been done in this way in the evaluation of streptomycin, PAS, isoniazid, some of the newer antibiotics, cortisone, corticotrophin and various drugs used in the treatment of rheumatic diseases and rheumatoid arthritis. In addition, the application of statistical skills in the clinic has been decisive in exploding the claims made for certain methods of treating minor ailments, such as the common cold.

What Green has to say is expressed mostly in general terms, and he presents an overall picture of great interest. Those who wish to know more of the detailed approach to the evaluation of a particular new drug should read the report of a conference on therapy involving members of the Department of Pharmacology and Medicine of Cornell University Medical College and New York Hospital.[1] At this conference was brought out the difficulty of comparing the response to a particular pharmacological agent in a group of patients, since the same person may respond quite differently to a drug under different circumstances. This is graphically illustrated in William J. Grace's description of observations on a man with a gastric fistula. The responses of the gastro-intestinal tract of this subject during various mood and feeling states could be watched and noted, and it was found that the response to food and to various drugs differed according to the subject's mood. These experiments, it was pointed out, all go to show that in evaluating a drug one needs to know not only the nature of the drug and the dose, but also the state of the individual at the time when the drug is given; and, as Harry Gold commented, similar observations can be shown to apply to responses of the blood pressure, the heart, or any other functional system in the body, and the patient's mood or attitude must always be taken into account. In the comparison of one drug with another, special attention was directed to the use of the placebo, the double-blind test (in which neither the patient nor the investigator knows which patients have received the drug and which the placebo), statistical analysis of the data and experimental design to eliminate bias. In his summing up of the conference, Gold referred to the emphasis placed upon the unconscious bias of the physician, "a subtle mechanism, which contrary to his best intentions may give rise to misleading results". He stated that it was a noteworthy feature of the various discussions that the control of this factor by the double-blind test was now recognized as imperative for the valid evaluation of medicinal agents, not only in the study of subjective symptoms such as cardiac pain, but also in studies involving so-called objective measurements such as those of iron in anæmia, diuretic agents and anticoagulants in thrombotic diseases. In his concluding words, "the conventional design of the treated and untreated groups in a clinical evaluation of a medicinal agent is giving way to the plan which calls for treating all patients, where possible, with the agent in question or with a placebo, the two being indistinguishable in physical form or appearance and their identity unknown to patient or investigator during the experiment".

To conclude this discussion we may with advantage return to Green's paper and his remarks on the ethics and limitations of clinical trials. He points out that in the trial of a common cold treatment in volunteers who have been told that they may or may not receive the test substance, no ethical difficulties arise provided that the investigator is satisfied that both the test and the control material are safe. However, in tests of a new remedy which may make the difference between life and death or between prolonged illness and swift recovery, the ethical problem is real. In this case, Green considers that, first, the doctor must never give his patient any treatment which he would not be willing to take himself in similar circumstances, and, second, he must be genuinely agnostic about the value of any remedy of which he contemplates making a controlled test. Once, however, a doctor is convinced in his scientific conscience that a new treatment which is freely available not only represents a substantial advance upon earlier methods but is unlikely to cause harmful side effects, he cannot, in justice, refuse to give it to any patient he believes to need it. On the other hand, when the value of a treatment, new or old, is doubtful, there may be a higher moral obligation to test it critically than to continue to prescribe it year in, year out with the support merely of custom or of wishful thinking. The College of General Practitioners in Great Britain is apparently contemplating doing some useful work in this field in evaluating various remedies for common ailments that have been used for generations. A limitation of even the best planned clinical trial is that it can hardly be of sufficient scope and duration to disclose the risk and incidence of long-term toxic effects and other side effects which have sometimes emerged after the prolonged use of certain powerful medicaments of the present day. It is in this field that the practising doctor, by careful observation and recording of his results, can make a valuable contribution. As Green points out, the doctor using the drugs in routine treatment has the ultimate responsibility for the care of the individual patient. "The most that the scientific investigator concerned with results in groups other than individuals can do is to show the doctor that the odds are heavily in favour of a remedy being safe when used as directed, and of its indeed doing what he wants it to do and nothing more."

[1] *Am. J. Med.*, November, 1954.

Current Comment.

NUTRITIONAL FACTORS IN IRON-DEFICIENCY ANÆMIA.

MOST workers on iron metabolism in the United States agree that, in the absence of hæmorrhage, nutritional factors have little part in the pathogenesis of iron-deficiency anæmia. Iron is excreted in such small amounts

that a positive balance should be seen with very small intakes. It is claimed that iron deficiency occurs as a result of nutritional defects only when requirements are increased by growth or by chronic hæmorrhage. This view is not held by many observers in other parts of the world. C. V. Moore[1] has tried to obtain more exact information about iron absorption and iron loss by using radioactive iron. In order to get as near normal iron intake as possible radioactive iron was injected into hens so that the eggs produced contained the isotope. After several weeks the hens were killed, so that their livers and muscles might be fed to subjects. Vegetables were grown in nutrient solutions containing radioiron. The subjects of the experiments were normal healthy students or laboratory personnel and patients with iron-deficiency anæmia. A striking observation was that the amount of iron absorbed from food ingested by normal subjects was 10% or less in most cases. Patients with iron-deficiency anæmia absorbed much larger amounts of the ingested iron up to 64%. An interesting observation was that the addition of 200 to 250 millilitres of orange or grapefruit juice more than doubled the percentage absorption of iron. The addition of ascorbic acid in relatively large doses greatly increased the iron absorption. Thus in an anæmic patient with eggs alone as the source of radioactive iron, about 5% was absorbed; while when one grain of ascorbic acid was given in addition to the eggs, over 70% was absorbed. Unfortunately all the experiments were acute; there is no history of the condition of the subjects in regard to ascorbic acid, and it is not known whether prolonged administration of ascorbic acid would have a like effect. It is commonly considered that absence of hydrochloric acid in the stomach causes poor absorption of iron. In patients with achlorhydria given 60 millimetres of 0·1N hydrochloric acid there was no improvement in the iron absorption. In the United States of America iron salts are commonly added to wheat flour for making bread. To the iron salts commonly used for this purpose radioactive iron was added, and these were baked in bread. The iron absorbed from the bread by 28 of 32 healthy subjects varied from 1% to 12%. The other four subjects absorbed 26% to 38%, but their iron stores were probably low.

Attempts were made to determine the iron loss from the body. The isotope in tracer amounts was injected intravenously, and the fæces were examined over a period exceeding one hundred and twenty days. Fæcal excretion for normal subjects varied from 0·3 to 0·5 milligramme per day. For iron deficiency patients the value was about one-tenth as much. Owing to several difficulties these figures are only approximate.

The author tries to estimate from the data obtained in the investigation how long it would take for a normal male and normal post-menstrual female to lose sufficient iron to reduce the hæmoglobin value to 7·5 grammes per 100 millilitres, assuming that no iron was taken in the food and there were no hæmorrhages. He arrives at the figures of six years and four years respectively. The average American diet contains 12 to 15 milligrammes of iron per day; therefore with a 5% to 10% absorption 0·6 to 1·5 milligrammes of iron would be absorbed per day. The amount lost from the body seems to be between 0·5 and 1·0 milligramme. The added requirements of children and young menstruating women place them in a precarious state of iron balance, so that poor diet and poor absorption can lead to the production of hypochromic anæmia. This question needs to be gone into much more thoroughly in view of the results noted in this and other recent papers.

The tables of dietary requirements of the National Research Council in the United States of America have up till recently recommended that 12 to 15 milligrammes of iron should be taken daily. As a result of much recent work the National Research Council now gives no figure for iron requirements on the grounds that we have no data and any figure would be a guess. It is difficult to get a daily diet of natural foodstuffs which contains 15 milligrammes of iron. To get this one would need to eat meat twice a day and liver once a week in the ordinary Australian diet.

[1] *Am. J. Clin. Nutrition*, January-February, 1955.

ACUTE POISONING WITH IRON SALTS.

A RELATIVELY common form of acute poisoning in young children follows the ingestion of iron preparations, usually in sugar-coated tablets. From three to ten grammes of ferrous sulphate have proved fatal in young children. Medicinal iron preparations are usually considered to be harmless, and no special precautions are taken to keep them from children. However, the margin between therapeutic and toxic doses of iron salts is smaller than is generally assumed. Although a number of cases have been described, little attention has been given to the toxic effects of iron absorbed from the intestine. M. A. Luongo and S. S. Bjornson[1] have described the effects of excess ferrous sulphate, in particular on the liver, in three fatal cases in children. The children were under two years of age, and each had swallowed an unknown number of ferrous sulphate tablets. The symptoms of poisoning came on very soon after ingestion of the tablets. The principal effects were vomiting followed quickly by profound shock, coma and death within thirty-six hours of taking the tablets. Anuria and Cheyne-Stokes breathing were also observed. With the ingestion of small doses of iron salts there is very little absorption from the intestine. In these cases the mechanism which controls the absorption of iron must have broken down completely, although at autopsy there was little if any visible damage to the intestinal mucosa apart from the fact that it was stained deep brown. In one case there was considerable œdema of the stomach mucosa. The striking change in each of the cases was in the liver. Grossly the liver did not show much change, but histologically there was seen a hæmorrhagic periportal necrosis or zonal necrosis. The cells in the central parts of the lobes showed little change. These changes in the liver must occur very rapidly, for they were well marked in one child, who lived only four hours after the ingestion of the tablets.

Luongo and Bjornson also fed rabbits with large doses of ferrous sulphate and observed the results. In rabbits given solutions of ferrous sulphate by stomach tube doses of less than 0·75 gramme per kilogram of body weight were apparently non-toxic; for when killed at varying intervals after the administration, the rabbits showed no pathological changes. Doses of 0·75 to 1·0 gramme per kilogram regularly resulted in hepatic lesion, although not always in death. Those animals killed at the end of five and six days showed little evidence of necrosis, but all animals up to nine weeks showed some hepatic fibrosis.

K. R. Reissmann, T. J. Coleman, B. S. Budai and L. R. Moriarty[2] carried out similar experiments on animals. They found that the lethal dose for both rabbits and dogs was about 200 milligrammes per kilogram of body weight. A significant rise in serum iron level was noted as early as ten minutes after administration of the iron solution by duodenal tube, and in dogs which received a sublethal dose the serum iron level remained elevated for one to three days. With large doses of iron the serum iron content was 40 to 50 times the normal figure. In neither dogs nor rabbits were any pathological changes seen in the intestinal mucosa after large doses of iron, and the absorption of copper and glucose was at the normal rate. Considerable hæmorrhagic changes were seen in the lungs in animals, where aspiration of irons salts was impossible.

K. R. Reissmann and T. J. Coleman[2] also studied the metabolic, respiratory and circulatory effects of absorbed iron salts. In all animals given excess iron salts very marked hyperventilation developed within the first hour after ingestion of iron salts. This was caused by a profound acidosis that developed rapidly with blood pH values as low as 6·7. The conversion of absorbed ferrous salts to ferric salts appears to be mainly responsible for the acidosis. The respiratory changes were those seen in metabolic acidosis. The cardiac output decreased progressively, but a normal blood pressure was maintained by arteriolar constriction until final collapse occurred.

[1] *New England J. Med.*, December, 1954.

[2] *Blood*, January, 1955.

Reissmann *et alii* do not describe the liver necrotic changes noted by Luongo and Bjornson, but the largest dose given by Reissmann *et alii* was 750 milligrammes per kilogram of body weight, at which dose Luongo and Bjornson also found no liver necrosis. The question may be raised whether the large doses of iron frequently given to patients with poor hepatic function may not constitute a danger. The healing and subsequent fibrosis of a portal necrosis would quite probably lead to diffuse fibrosis and possibly the development of cirrhosis.

PSYCHOGENIC RHEUMATISM.

"RHEUMATISM" used to be described as "a muck heap of diagnoses". Today, much of that heap has been sorted out and one of the finds has been "psychogenic rheumatism". Recently, the Royal Society of Medicine[1] held a discussion on this syndrome and its management; despite objections to its name on the grounds that it implies an organic disorder which does not exist, it would seem that the name is likely to persist since it is a conveniently comprehensive description based on the postulate that emotional conflicts may bring about somatic disturbances manifested as pain and stiffness. But it is important not to let the current fashion for psychosomatic diagnoses take full charge; only too often are they arrived at after an incomplete examination, or because of an incomplete differential diagnosis (both based on laziness, which is literally a deadly sin in medicine). During the discussion, Ernest Fletcher and J. H. Jacobs[1] recounted instances wherein actual organic disease was overlooked in patients who were emotionally unstable; they also pointed out that ankylosing spondylitis, osteoporosis, fibrocystic disease, several neurological conditions and certain tumours frequently present, in their early stages, with pain but without any physical signs. It is generally agreed that psychogenic rheumatism can be classified in three types: (i) Psychopathic exaggeration of trifling organic disease in which the hysterical symptoms become completely predominant and bury the original symptoms of the underlying disease. (ii) Prolongation of the symptoms of some organic disease which is long past and done with. (iii) Somatic symptoms which are entirely psychogenic, arising *de novo* from primary emotional conflict. The common feature of these types, more prominent than in other stress disorders, is the utilization or exploitation of the symptoms for some purpose in the life of an agitated or inadequate personality—but always this motivation is kept more or less out of the consciousness, and thus a formidable barrier is raised to treatment. The more useful the symptoms are to the patient the less is any likelihood of cure. Moreover, the symptoms may be so realistic that the patient develops habits of prolonged muscular fixation with consequent ischæmia and ultimately fibrosis, so that pain which commenced as a somatic manifestation of a functional disorder ultimately becomes organic and irreversible.

Much of the discussion was concerned with treatment and, as might be expected, nothing definite emerged. The psychiatrists stated that repeated and prolonged physical examinations tend unduly to fix the importance of the condition in the mind of the patient. Yet how can the diagnosis of psychogenic rheumatism be arrived at without exhaustive examination? There were also complaints that once the patient's symptoms have been accepted at face value and been given a diagnostic label by, say, a general practitioner, and once physiotherapy or some similar treatment has been instituted, the patient is confirmed in his belief in the organic basis of his troubles and cannot be disabused of it. This again seems to be rather unfair to the general practitioner. It might almost appear that the condition is one which must be accepted as being too firmly fixed for psychotherapy, and that P. E. Sundt[1] may have been right in suggesting that it is better to allow such a patient to have a definite if incorrect diagnosis rather than to attempt to give him insight; and that William Tegner's[1] summing up was a just one: "What can be done about these patients who in turn exhaust general practitioners, consultants, psychiatrists and physiotherapists? The answer is nothing; they will always be with us, and the burden must be shared in turn by all the team."

[1] *Proc. Roy. Soc. Med.*, February, 1955.

THE PROPHYLAXIS OF CARDIAC INFARCTION.

IF it can be assumed that patients with coronary artery disease will normally go on to suffer coronary occlusion and infarction, then the work of Claude S. Beck and David R. Leighninger,[2] in their article "Operations for Coronary Artery Disease", can surely be regarded as of prophylactic value. Beck and Leighninger found that if dogs' hearts were given extra blood supply, and later had the coronary arteries ligated, both mortality from the arterial occlusion and subsequent development of infarction were tremendously reduced by comparison with the results of ligating the arteries without preliminaries. Their experiments show that although normally there is no connexion between the coronary arteries, interference with the coronary circulation stimulates the development of what they call "intercoronary channels". Coronary occlusion itself stimulates this development, the question of survival depending on the extent of the infarct and the amount of disturbance of the cardiac mechanism, and so on the time available for the development of intercoronary channels before the heart muscle fails. The authors also show in dogs that mere trauma due to operating on the heart can stimulate similar development. They have used two operations, the first a grafting of the pericardium with its vessels onto the heart wall, the second a vein graft between the aorta and the coronary sinus; in each case, the coronary sinus where it enters the right auricle is partly occluded with a loose ligature so as to induce back pressure through the capillary bed. After a time, however, the intercoronary channels develop and take over the circulation. Although there cannot be, by this means, any recanalization of occluded vessels or regeneration of infarcts or halting of progressive degeneration of diseased vessels, Beck and Leighninger claim that the performance of either operation in patients with progressive coronary disease will so increase the quality of the myocardial circulation that when the ultimate occlusion happens the result will not be disastrous. Since the mortality of the operation is reasonably low, it might be justified for patients with disabling, painful and progressive coronary disease.

ATOMIC RADIATION AS AN OCCUPATIONAL HAZARD.

THE total number of establishments concerned with the handling of radioactive products is at present very small; nearly all of them are huge plants engaged in the primary processing of sources of atomic energy, and their large staffs of employees for the most part have technical education and training which enable them to appreciate the dangers of atomic radiation and to cooperate successfully in the necessary safety measures. Even so, when the devastating potentialities of wayward radiation are considered, it is remarkable that the record of the atomic industry with regard to occupational morbidity and mortality is considerably better than the average for industry generally. In "Personnel Protection in Atomic Industry" W. D. Norwood[3] discusses these figures and the safety measures that, in a plant employing 9000 men and women in the production of plutonium, have ensured that there has not been a single injury due to radiation in ten years of operation. A new character, the health physicist, occupies the centre of the stage. He is responsible for protecting workers against excessive exposure to radiation; he and his team of physicians, engineers and physicists are concerned with isolating and shielding

[1] *Proc. Roy. Soc. Med.*, February, 1955.
[2] *J.A.M.A.*, November 27, 1954.
[3] *Arch. Indust. Health*, January, 1955.

radiation, controlling the escape of liquid or gaseous radioactive wastes and the disposal of solid wastes, monitoring every section of the plant and every employee's clothing, measuring the radiation to which employees have been exposed to see that it does not exceed safe limits, and maintaining the training of the employees in safety precautions. Perhaps even so extensive and exacting a task is less difficult in the circumstances, when the magnitude of the risk is great and when everybody is continuously aware of the risk; but the imminence of the extension of radioactive processes outside the atomic plants into more or less everyday life brings up the question of whether everyday life is prepared to meet the consequent risks. Already many hospitals, for instance, are equipped with quantities of potent radioactive materials; atomic power for transportation is being tested, the waste heat from atomic reactors is about to be utilized in industry, and the method of using radioactive waste materials as a source of energy for small engines is being perfected. Inevitably much potentially dangerous material will be distributed at large among the general population; much of it will be handled by persons ignorant or careless of its capabilities, and there will be few health physicists to watch over it—merely lay safety officers not under the constant urgent pressure of continuous risk to keep them alert, but only needed from time to time and likely to become careless as a consequence. All this and more will happen within a comparatively few years. Consideration of the present record of industry in general, with a morbidity rate approximately twice that of the atomic industry in spite of the infinitely greater risks of the latter, leads to the hope that the public in general, and the people who will be responsible for the management of radioactive projects in particular, will receive adequate training in safety precautions, and that the medical profession will be trained in the recognition and treatment of the effects of excessive radiation.

INTRAVENOUS CAFFEINE THERAPY FOR HEADACHES.

AN interesting analysis of headaches met with in general practice has been made by Allen S. Johnson[1] in an article entitled "The Headaches of Medical Practice". Using Wolff's classification of the ætiology of headaches, he found that among 100 consecutive patients, 74 seemed to have intracranial or extracranial vascular distension as the basic mechanism of their headaches, 15 had cranial or ocular muscle spasm, and 11 nerve irritation. The actual diagnoses of the original conditions ranged from acute cervical myositis through gastro-intestinal dysfunction, hypertension and migraine to nervous and emotional tension; but Johnson indicates that it is not the original condition but only the mechanism by which that condition causes headache which should determine the selection of measures designed to relieve the headache. If this is so, then caffeine, with its double action producing ultimately a predominant vasoconstriction in the cerebral blood vessels, but a slight vasodilatation in the peripheral vessels, can have only a limited application in the treatment of headaches. In the post-traumatic syndrome, and in hypertension without encephalopathy, which cause distension of cranial arteries, only transient relief can be expected; in migraine, which causes both intracranial and extracranial vascular distension, the effect would vary; in intracranial distension due to such conditions as anoxia, fever and sepsis, emotional states, post-alcoholic distress, the effects of lumbar puncture and nitrites, constipation and even subarachnoid hæmorrhage or brain tumour it may be expected to have a good effect. In practice, when 500 milligrammes of caffeine and sodium benzoate are given intravenously, it appears that the results are substantially in agreement with those expectations, though various authorities report widely divergent results; perhaps the fact that in man, as compared with laboratory animals, the effects of caffeine are remarkably inconstant, may account for this divergence. However, it is obvious that for several of the above conditions caffeine should not be necessary, since treatment of the condition would promptly relieve the headache. Moreover, in all the series of cases quoted by Johnson, emotional tension far outweighs all the other causes of headache, and suggestion in many instances or the substitution of placebos in others has had as much effect in producing relief as has caffeine; whether it is justifiable to venture upon the relatively complicated procedure of intravenous injection for simple emotional upsets when a homely cup of tea would probably do as much good is worth considering. In any case, Johnson's final summing up is very sound—"it is probable that for some time to come the symptomatic treatment of headache will depend on aspirin, sedation and sympathy—augmented when necessary with codeine".

[1] *New England J. M.*, January 20, 1955.

CIGARETTES, WHISKY AND CORONARY DISEASE.

IN the course of an article on the relationship between smoking habits and death rates, E. C. Hammond and D. Horn[1] indicated that deaths from coronary disease were much more common among cigarette smokers than among non-cigarette smokers. This inspired I. E. Buff[2] to investigate the effect of cigarette smoking on normal persons as shown by the ballistocardiograph. He found that among 194 men and women between twenty and thirty years of age, nine (5·1%) showed abnormal changes in their ballistocardiograms after smoking one cigarette, and among 206 aged between thirty and forty years, 33 (16%) showed similar abnormalities. These figures have nothing to do with coronary disease (although if the patients could be followed up, some very useful data might be obtained), but they serve as a useful comparison with tests done on 28 normal persons by H. I. Russek, B. L. Zohman and V. J. Dorset[3] and reported in "Effects of Tobacco and Whisky on the Cardiovascular System". These 28 subjects were all habitual smokers who had had vague symptoms attributed to smoking, though none had coronary disease; 16 showed significant electrocardiographic changes after smoking. Administration of glyceryl trinitrate made no difference to these changes, which suggests that they were not due to coronary vasoconstriction. Changes of much lesser magnitude were observed after smoking "denicotinized" cigarettes from which about 51% of the nicotine had been removed. Among 37 patients suffering from coronary disease, none showed significant changes in the electrocardiogram after smoking, although 18 had significant deterioration in their ballistocardiographic pattern, which improved slightly after glyceryl trinitrate was administered, but which improved significantly after 30 to 60 cubic centimetres of whisky were administered. In both normal persons and those with coronary disease, the smoking of cigarettes produced a significant increase in heart rate and blood pressure. The first conclusion to be drawn is that numbers of normal persons suffer from cardiac sensitivity to nicotine and it seems that the mechanism of this is due not to coronary vasoconstriction, but probably to direct action on the myocardium. Secondly, since smoking does not upset the electrocardiograms of patients with coronary disease, but does cause ballistocardiographic changes which are unaffected by glyceryl trinitrate, but are antagonized by whisky (which has a peripheral vasodilative action only), it is suggested that while nicotine has no coronary vasoconstrictive action, it has a peripheral action which adversely affects the heart in coronary disease. Whisky, we know, dilates the peripheral vessels and is commonly allowed or prescribed for persons with high blood pressure or for subjects complaining of precordial pain possibly due to a cardiac condition. Apparently we should be right to advise moderation in the use of tobacco if not its discontinuance, but we need not frown upon the patient with precordial pain, possibly of cardiac origin, if he claims that whisky does him good.

[1] *J.A.M.A.*, August 7, 1954.
[2] *J.A.M.A.*, February 12, 1955.
[3] *J.A.M.A.*, February 12, 1955.

Abstracts from Medical Literature.

RADIOLOGY.

Intraosseous Venography of the Lower Limb and Pelvis.

A. C. BEGG (*Brit. J. Radiol.*, June, 1954) describes a new method of ascending venography of the lower limb and pelvis in which the contrast medium is injected into the medulla of an appropriate bone. The selection of the site of injection depends upon the particular problem involved. To demonstrate the internal iliac vein the common iliac vein and the inferior *vena cava*, the great trochanter has proved to be the most suitable; to show the superficial and deep veins of the thigh and the external iliac vein, the tibial tuberosity has been found satisfactory; while to show the venous systems of the leg and thigh, the lower end of the tibia has proved most suitable. If this last-mentioned site is covered by an ulcerated area, the lower end of the fibula may be used. The *os calcis* has not proved to be so useful, for its deep drainage seems to be almost confined to the post-tibial vein. These sites are readily available no matter how swollen or œdematous the leg may be. During injection the contrast medium passes out with extreme rapidity from the bone marrow, through the cortex and periosteum, to reach the deep and superficial veins. These numerous periosteal channels so flood the venous system that a better concentration is obtained in the larger veins than that which follows even a rapid intravenous injection. "Uriodone" is removed from the marrow almost immediately and rarely spreads more than a few centimetres from the point of the needle, however quickly the injection is made. The scope and value of the method and its advantages are illustrated by reference to cases of acute deep thrombophlebitis, gravitational ulceration and skin diseases. Intraosseous venography has proved to be a safe, simple, flexible and certain method of demonstrating the deep, superficial and communicating veins of the leg and pelvis. It is quickly carried out under local or short "Pentothal" anæsthesia and is thus suitable as a form of out-patient examination. Both legs may be investigated at a single session; 20 millilitres of 50% "Uriodone" solution are used for each leg. The examination may be completed in five minutes. Thirty patients have been investigated without incident.

The Oral Administration of Barium in Acute Obstruction.

J. FRIMANN-DAHL (*Acta radiol.*, October, 1954) states that in all doubtful cases of small bowel obstruction, an X-ray examination of the bowel by means of barium administered by mouth should be carried out. The possibility of obstruction is no contra-indication to the procedure. In cases of stenosis of the large bowel, barium enema examination is the method of choice, since barium suspension given orally has a tendency to become inspissated when water is resorbed from the colon, and an incomplete obstruction could just possibly be rendered complete. With small bowel obstruction the contrast medium becomes more and more diluted, the nearer it reaches the site of the stenosis. Consequently, what occurs is precisely the opposite of that generally believed. In the small bowel it seems impossible for the barium to become thickened and dangerously increase the degree of obstruction. It is all-important to decide from the routine films whether the obstruction is situated in the small or the large intestine. If large bowel obstruction is most likely, the approach to a definite diagnosis is the barium enema examination. However, in some instances it is impossible to decide in which part of the tract the stenosis is situated. This happens when the small intestine is greatly distended and the mucosal pattern nearly obliterated. A barium enema should then also be given and an examination of the large bowel carried out. Should the lumen be clear, the obstruction must obviously lie in the small intestine.

Arteriography of the Digital Arteries in Raynaud's Disease.

R. B. LYNN, R. E. STEINER AND F. A. K. VAN WYK (*Lancet*, March 5, 1955) prepared arteriograms of the digital arteries of the hands of 23 patients who had intermittent spasm and colour changes of the fingers. They state that two groups of patients emerged from this study: (i) those with anatomically normal digital arteries, and (ii) those with obliteration of the digital arteries. The two groups are clinically separable, since those with digital artery obliteration have nutritional changes in the fingers. The authors consider that the term Raynaud's phenomenon should be retained to designate intermittent spasm of the digital arteries without clinical complication and with a normal arteriographic appearance of the digital arteries. "Thrombotic digital-artery disease" is regarded as a better term when local nutritional changes are present and there is arteriographic evidence of obliteration of the digital arteries. The authors state that they have no histological evidence of the underlying pathology in the digital arteries of these patients, but such changes as do take place are non-specific. This distinction is important in deciding treatment because the patient with Raynaud's phenomenon does well when treated with vasodilator agents such as "Tolazoline" and sympathectomy, whereas in cases of thrombotic digital artery disease little can be done to improve the circulation. Improvement following sympathectomy is slight, and early relapse is the rule. Arteriography is a safe and satisfactory method of distinguishing between these two groups of patients.

The Potential Hazard of Enemas with Hirschsprung's Disease.

H. L. STEINBACH, R. H. ROSENBERG, M. GROSSMAN AND T. L. NELSON (*Radiology*, January, 1955) state that severe reactions and deaths have occurred not infrequently in patients with Hirschsprung's disease during or immediately after administration of an enema. The cause of these reactions has not been conclusively demonstrated, but some evidence has been provided to suggest the possibility of water intoxication due to rapid absorption of water from the colon. It is also possible that reflex cardiac inhibition and shock may be produced by abnormal distension of the colon. Megacolons have a much larger absorptive surface than normal colons, and multiple superficial ulcerations of the mucosa are frequently present, both factors adding to the rate of absorption. Absorption from the intestine has been shown to vary directly with the hydrostatic pressure of its contents. The hypertrophied muscular wall and partial obstruction to evacuation produced by the "aganglionic segment" of a megacolon are capable of producing a very high intraluminal pressure. Because of the usual presence of a large amount of fæcal material that interferes with filling, it is common practice to use a high hydrostatic pressure in introducing enemas in these cases; this further increases the intraluminal pressure. "Prostigmin" and similar drugs, often used in these cases, also increase the muscular contractions of the colon. It is recommended that isotonic saline solution be used in enema studies in patients in whom Hirschsprung's disease is suspected. It is also recommended that the smallest amount of solution necessary be introduced under low pressure, and that as much as possible of the fluid be recovered after the procedure has been completed.

Pulmonary Appearances in Polyarteritis Nodosa.

BASIL STRICKLAND (*J. Fac. Radiologists*, January, 1955) states that while the cause of *polyarteritis nodosa* is still unknown, it would appear from experimental evidence in animals and clinical observation that the disease is a manifestation of anaphylactic hypersensitivity to various antigens, and it is of interest to note that in 15% of cases the patients have a past history of some allergic phenomenon. Pathologically the disease is a necrotizing inflammatory obliterative lesion of the small arteries, arterioles and occasionally veins. Microscopically there is a segmental necrosis, which begins in the media and always involves the internal elastic lamina; in association with this there is an inflammatory exudate containing fibrin and eosinophile cells. This is the fundamental abnormality, and all other changes are merely complications of this basic lesion; these include thrombosis with organization and recanalization, aneurysm formation (with or without rupture) and healing often with deforming fibrous scars in the arterial walls. *Polyarteritis nodosa* may affect either sex at any age, but is most commonly seen in males between the ages of thirty and forty years. The average duration of the disease is from six to twelve months, but this again is variable. In over 50% of cases the condition starts with an acute febrile illness, while in the remainder the patients have fever during some part of the disease, tachycardia often being out of proportion to the fever. The kidneys are almost always involved, with the presence of albumin, casts of all types and red cells in the urine. Sometimes the clinical picture is one of acute nephritis, which progresses to uræmia within a fairly short time. The occasional occurrence of massive hæmaturia is due either to rupture of a vessel or to a large renal infarct. Hypertension is common and variable in character; œdema may be cardiac or renal in origin. The course of the illness is quite unpredictable and tends

to be punctuated by a series of apparently unrelated incidents due to the involvement of the arteries of various organs. The one persistent clinical feature common to the author's series of cases was the presence of a well-marked respiratory illness dominated by cough and dyspnœa. From the radiographic viewpoint attention is drawn to the bizarre nature of the pulmonary opacities, their transience and their tendency to appear first at one site and then at another, often progressing in one lung field while simultaneously regressing in the other, usually leaving a normal appearance once resolution is complete. The opacities may coalesce or remain discrete; they may be dense and homogeneous or of extremely low density and irregular; the very lack of pattern seems almost a typical feature in itself. By far the commonest radiological findings in *polyarteritis nodosa* are those due to cardiac failure with or without pulmonary œdema.

PHYSICAL THERAPY.

Lesions of Uterus and Vagina.

R. E. FRICKE AND M. VAN HERIK (*Radiology*, September, 1954) state that their interest was aroused by finding a case of primary lymphosarcoma of the *cervix uteri* which responded satisfactorily to radium therapy, and they undertook a review of the rare pelvic cancers treated at the Mayo Clinic between 1935 and 1944. Radiotherapy was found to have played a minor part in the treatment of these cancers, as nearly all were types known to be resistant to irradiation. During the decade under study 1273 malignant tumours of the *cervix uteri* were treated; only two of these were unusual, and these were both hæmangio-endotheliomata. The first patient was treated by total hysterectomy and remained well after twelve years. The second patient was treated with radium and died from pulmonary metastases two years after treatment; the local lesion remaining apparently clear. Approximately 116 patients with primary malignant tumours of the vagina were reviewed. Of this number five showed unusual lesions. The first was an infant of two years with a *sarcoma botryoides*, which showed temporary response only to palliative radium treatment. Two patients were found to have melanotic tumours. Combined surgery and irradiation were used, but both patients died within about a year. It is considered that in these cases surgery offers the only hope of cure as melanotic growths are extremely radioresistant. The remaining two patients had Grade III leiomyosarcomata of the vaginal wall. Treatment in one case was by irradiation alone, and in the second case by a combination of radiotherapy and surgery. Both patients died after about three years from malignant disease. Of 789 cases of malignant disease in the *corpus uteri*, 20 proved to be other than the usual adenocarcinoma. One patient had a chorionepithelioma; 17 were diagnosed as suffering from leiomyosarcoma, one from mixed mesodermal tumour and one from carcinosarcoma. The myosarcomata were regarded as likely to be radio-resistant, and treatment was mainly surgical, in some cases with post-operative irradiation. The results were not good, as 13 of the 20 patients died within the first five-year period. Some doubt is cast on this assumption by the result obtained in one case of myosarcoma, in which radiotherapy was used for extensive post-operative recurrences, and the patient survived for five and a half years. If operation presents much risk, irradiation may give worthwhile palliation.

Hodgkin's Disease.

R. J. HEALY, H. I. AMORY AND M. FRIEDMAN (*Radiology*, January, 1955) review 216 cases of Hodgkin's disease treated at the Walter Reed Army Hospital, Washington. In every instance the diagnosis was established by histological study of an excised lymph node. In 74% of the patients in this series the first sign of the disease was enlargement of a lymph node in the cervical chain, generally the lower part of the neck. The authors state that this lends support to the belief that Hodgkin's disease is unicentric in origin. They emphasize the fact that early diagnosis and aggressive treatment are important. The diagnosis can be made only by excision biopsy of a diseased lymph node. Any lymph node, especially in the cervical chain, which remains enlarged for three weeks or longer should be excised for histological study, except in the presence of an inflammatory lesion as cause of the adenopathy. In this series of cases the absolute five-year survival rate was 37%, and 63% of the cases were advanced. Many of the patients with widespread disease have survived five years; examples are given with details of the cases. The authors state that these results substantiate the opinion that in Hodgkin's disease the primary treatment should be aggressive X-ray therapy; it is important to deliver a tumour dose of 1500*r* in one week or up to 2500*r* in three weeks, and for some of the more resistant lesions a total tumour dose up to 4000*r*. In early cases the entire group of involved lymph glands should always be treated through a large field, and in the more advanced cases the adjacent group of lymph glands as well. For large deep-seated tumours in the thorax or abdomen supervoltage X-ray therapy is decidedly helpful. All patients in this series were treated primarily with X-ray therapy. A small percentage, about 10%, were also given nitrogen mustard at some time during the course of their illness.

Graves's Disease.

P. O. GEDDA AND M. LINDGREN (*Acta radiol.*, September, 1954) describe the manifestations and technique of treatment of the hyperophthalmopathic type of Graves's disease. They state that the eye changes usually dominate the picture, while the basal metabolic rate may be increased, normal or decreased. The orbital picture is characterized during the acute phase by pronounced œdema of the fatty tissue, of the connective tissue and of the eye muscles, with infiltration of round cells, especially lymphocytes. The changes produce an increase in the retrobulbar pressure and protrusion of the eyeballs—true exophthalmos. Many observations favour the suggestion that the picture is ascribable to increased production of the thyroid-stimulating hormone of the anterior lobe of the pituitary gland. In 19 cases of this type of Graves's disease the patients were treated by X-ray therapy; 16 received irradiation of the hypophysis and orbits, and three of the orbits only. The hypophysis was irradiated through four temporal fields, two on each side; a dose of 1500*r* was given to each field in the first series, and five weeks later 600*r* to 900*r* in a second series. The depth dose was 3000*r* to 4000*r* in sixty to ninety days. In irradiation of the orbits a lateral field was used, the lens being avoided; a total dose of 900*r* was given with a daily dose of 150*r*. A further series of treatments was given later. More than half the patients (11) had earlier been submitted to thyroidectomy because of hyperthyroidism. Of these, five still had signs of hyperthyroidism, as did a further five of those who had not undergone operation. In most cases treatment of the hypophyseal region produced satisfactory regression of the eye symptoms. This may be ascribed at least partly to direct irradiation of the posterior part of the orbits. That irradiation also suppresed the increase in thyroid-stimulating hormone is shown by the fact that it controlled hyperactivity of the thyroid in all ten patients with hyperthyroidism. It is important to diagnose the disease as early as possible and to start treatment without delay. The doses given produced no demonstrable effect on the normal functions of the hypophysis. Thyroidectomy, treatment with thiouracil compounds and radiotherapy of the thyroid gland are contraindicated in this type of Graves's disease.

SURGERY.

Patent Ductus Arteriosus.

IRENE S. CADE (*Brit. J. Surg.*, July, 1954) has reviewed 50 cases of patent *ductus arteriosus*. She states that in the United States of America it is now generally accepted that the presence of a patent ductus is in itself sufficient indication for surgery, with the exception of certain patients who are first seen in late life. In Great Britain, however, the advisability of surgery in all cases has not been universally accepted. The difficulty and dangers of the operation are increased if it is delayed until adult life, as the ductus becomes shorter with increasing age, adhesion about it becomes more dense, and the walls become more rigid and friable. The optimal age for operation is from five to ten years, but it may be carried out earlier than this if symptoms are manifest or if there is evidence of cardiac enlargement. There has been much discussion in the literature on the relative merits of ligation and division of the ductus. In the series of 50 patients presented by the author, simple double ligation with silk was the method of closure except in two patients in whom division with the suture was carried out. There was no death in this series, and the majority of patients have shown considerable improvement as a result of the operation. No proven recurrence has been noted. The author recommends that in all children in whom the *ductus arteriosus* is still patent at the age of six years, operation for ligation of the ductus should be carried out. The results indicate that adequate ligation is sufficient to prevent recurrence, and the more formidable operation of division is necessary only in rare cases.

On the Periphery.

MEDICINE'S UNHEEDED HANDMAIDEN.

No matter how primitive the people, how sunk in savagery and ignorance, how gross their habits, how childish their beliefs, music of a kind they have always made. Crude, it certainly must have been; shrill and discordant as it may have seemed to our ears, it was an essential emotional outlet for them, and at the same time an invigorating stimulus. Long before the existence of any organized artistic production, rhythm stirred the senses with a strange compulsion. The beat was bold, for savage music is essentially accentual. It was early associated with ceremony. Birth and death, war and peace, calamity and pestilence, the changing of the seasons, the raising of crops and the various propitiatory devices for influencing the gods, and man's emotions concerned with these, called for musical utterance, diversified by singing and dancing. And so, wherever one looks through the binoculars of anthropology and folk-lore, one sees this common conformity to some form of musical expression. Whether it be the measured beat of an Indian tomtom, the sistrum of Isis or the lute of Apollo, man's emotions have responded, his heart has quickened to a new fervour, his muscles have felt a new excitement as his untutored senses have come under the sway of rhythm's invisible promptings.

Music is the language of the emotions. Where words end, music begins; and when logic fails the progressions of harmony persuade; as if

> Some chord in unison with what we hear
> Is touch'd within us, and the heart replies.

It says what the mind cannot utter; it communicates the feelings which have no substance; it supplies a need which has no name. Our aural eroticism is early established, so that the ear has its pleasures which the mind cannot suppress. Every infant delights to beat its dish with a spoon and arouse its excitement with a rattle. Infant pleasures are primitive and undisguised. The baby registers its displeasure with a cry, its joy with a gurgle. But the child is father to the man and soon learns the secrets of aural narcissism by singing to itself. Its nursery songs identify its childish conflicts. When its security is threatened it satisfies its aggression through the shriek of a tin whistle or the unmusical blurt of a toy trumpet. One of its chief joys is rhythmic movement. It often creates its own by rocking and jigging for the mere pleasure of it. An acme of contentment is reached when its cradle is rocked or when, in the arms of a beloved parent, it is subjected to a similar rhythmic motion. A child's reactions to music are instinctive and compelling. Its attention is arrested by anything that makes music. Tiny feet are led into a dance whenever the barrel-organ plays in the street or some ragamuffin fiddles a tune; and small mouths are open in song when music comes from the wireless cabinet or an older child plays the piano. It stores up musical impressions and associations that other music may awaken in later life, as it marches happily to the drum and fife, finds enjoyment in class singing and knows joy when there is a song in the heart.

When the years bring care and long clothes the attitude to music may seem to alter. Spontaneity may give place to self-consciousness; but the fundamental urge for self-expression is not obliterated, and the adult who would blush to sing in public readily finds voice in the bathroom. Forces that know no other outlet come welling up from the larynx in the phonic cadence of a ditty. For the simple anonymous pleasure of singing may lift the hatch from the imprisoned wishes and repression may find resolution in a song. Thus, unmindful of the motive, the soldier joins in the canteen chorus, making himself hoarse with the vocal delights of a rousing tune; the hard-bitten sailor chants from the yard-arm; the choir-boy glorifies his Maker with a song that resounds through the vaulted nave; and the young mother, her face transfixed in adoration, sings a lullaby to the child in her arms. All feel the relief, the exultation that comes from turning their feelings into a tune, as when the morning stars sang together and all the sons of God shouted for joy. For there is magic in a madrigal and enchantment in a hornpipe. It is not necessary to listen to the symphonies of Beethoven or follow the fugues of Bach. They who wish may untwist the chains of harmony; but the open notes of a simple descant may touch the heart and unlock the lips. Music's idiom is as varied as it is widespread. It may come from fiddle or flute, from dance band or harmonium: it may be a sea chanty or a cradle song, a hymn or a "pop" tune; but there is in it something to set the feet to jig or to bring a glad whisper to the weary spirit. For many a maid has been induced to dance Canary with sprightly fire to the music of reed and rebeck; and many a man has felt his passions surge, tarantulated by a tune. Music makes the day's work pleasanter. It lends wings to the laborious hours and soothes the monotony of repetition. It increases strength and allays fatigue. It lifts up the spirit with invisible hands. The slave in the galley felt this power when he crossed the Ægean; the stone-mason knew it when he built the walls of Messena; the wherryman knew it on the Thames, the boatmen felt it on the Volga. Convict gangs sang to the clanking of their chains. They raised their voices at the treadmill and their song echoed in the slate-pits.

The legends of antiquity offer many examples of the power of music. The canticles of Apollo, for instance, moved multitudes; and all things hateful to Zeus trembled at the sound of music. None could resist the charm of Orpheus with his lyre, for even the animals and the rocks lent forward to listen, spellbound by his song. In the strategy of conflict music sometimes exerted a special force. For not only did the Israelites shatter the walls of Jericho with their trumpets, but the troops of Demetrius were successful in raising the siege of Argos with battering-rams urged on by the trumpets of Herodorus. When the Lacedæmonians went into battle a tibicen played soft music lest the fury of their passions caused disorder in the ranks. Tyrtæus, the lame schoolmaster, inspired the Spartan soldiers by his music; and Terpander, the Lesbian harpist, is said to have quelled sedition by the songs he sang and the music he played. Thaletas, the Cretan, is credited with curing a pestilence by his music. A minstrel guarded the chastity of Clytemnestra while Agamemnon was away. The lyre of Empedocles once prevented murder; and the tempestuous moods of Achilles were assuaged by a similar instrument. While the music of Damon's harp pacified the drunken soldiery, that of David exorcised the evil spirit from King Saul. For the charms that music hath to soothe a savage breast were well known before Congreve linked them with the power of softening rocks and bending the knotted oak, and long before the lovely Desdemona learned to sing the savageness out of a bear. The persuasiveness of music was recognized throughout the pagan world. It could soothe, but it could also stimulate. In the Phrygian mode it was known by the Greeks to impart a wild and maddening excitement, so that on one occasion the spirit of Alexander was so much agitated by the flute-playing of Timotheus that he seized his sword and commenced belabouring those about him. The castrated priests of Attis shouted in their frenzy and slashed themselves with knives when carried away by the corybantic rhythms of flute and timbrel. The Mænads with sado-masochistic delight carried on their orgiastic worship of Dionysus. Other less cultivated races in their corroborees and pagan festivals allowed the rhythm of music to incite their feelings and reacted with furious dances and boisterous behaviour which often ran beyond their control. And many a Dervish met his death through the beat of a drum.

It should occasion no surprise to know that music has formed part of every religion, though the plain-song of the early Catholic Church is a far cry from the barbaric revels of Cybele. But music melts the heart of the penitent and augments the prayer of the votary. It links the mind with the moving symbolism of the essential mystery. Whether as the stringed accompaniment of a Greek pæan, the simple flute-flowing melody of a Roman supplication, or the dramatically accentuated measure at the sacrifice, music has not only aided the expression of religious feelings, but has helped to create an ecstasy in which religious teachings have been more readily acceptable. Music lay close to the heart of the Hebrew, as with most oppressed people. It stimulated the voice of his prophets and wise men; it brought him dreams of freedom and the glory of heaven, and it lent a new expression to his adoration. He heard the sound of the tabret at the temple of Jehovah; but the melting pipe led his errant footsteps into the groves of Baal, though the prophets of his God came down from the high place with a psaltery and a pipe and a harp before them, prophesying as they came. The music which accompanied early religious ritual was meant to stir the feelings of the celebrant and those taking part in the service. It was meant to enhance the magic and the supernatural element upon which all divinity is built. And it did this because music and magic have a common bond and are complementary in their effect, and because music has a logic of its own, unrelated to the pros and cons of intellect, but nevertheless driving deeply into the unfathomable well of emotion.

With religion came healing. It is likely that the first healers were priests and that the first hospitals were

temples; so that incantation and music were the initial forms of treatment. Tradition asserts their success. Since the emotional force of music was realized and illness was believed to be spiritually conditioned, it was natural that music should be used as a therapeutic aid. The earliest Egyptian records favour music as an aid to female fertility. In the temple at Epidaurus in Argos the patients, in the great outer colonnade, dozed to the strains of music and song while they were healed by the sacred serpents, just as in the Moslem hospitals of the Middle Ages soft music was played to lull the sleepers. Asclepius is said to have cured deafness with a trumpet, and to have used the same instrument to relieve the pains of sciatica. Galen speaks of playing the flute "on" the affected part, implying the use of vibration therapy, rather than mollification by music. The ancient flute, descendant of the savage tibia, was no doubt a lenitive instrument, and is frequently credited with the power of curing disease or alleviating sickness. Among other illnesses it was said to be useful in the relief of epilepsy and sciatic gout. In this latter case the flute, according to Theophrastus, should be played in the Phrygian mode. It was not only specific for the bite of a viper, but, according to Democritus, if played properly, it could cure disorders of the mind. Xenocrates also employed the flute in his treatment of lunacy. In the opinion of Martianus Capella, the Carthaginian, fevers were dissipated by song; and Aristotle believed that music softened the rigours of punishment. There are many such references in the classics to the healing power of music in disease, and their perusal leaves little doubt that the healers and the healed believed firmly in the value of instrumental melody and song as potent curative agents.

Christianity, though it killed most things of the mind, apparently spared music, and its therapeutic use persisted to a degree through the dark ages. Records are few and incomplete; but here and there a reference may be found, as when we read of Henri de Mondville solacing his patients "on a ten-stringed psaltery". Music was often employed in the fourteenth century to quell the dancing manias; and in the seventeenth century tarantellas were specially written for the mass hysteria of those believed to have been bitten by a tarantula. Rabelais refers to the curing of the sick with a song; and Robert Burton pays homage to music in the treatment of melancholia. Samuel Johnson's contemporary, Dr. John Armstrong, who wrote on "The Art of Preserving Health" in four long unrhymed cantos, was of the opinion that

> Music exalts each joy, allays each grief,
> Expells diseases, softens every pain,
> Subdues the rage of poison, and the plague.

Where, then, does music stand in the health programme of today and amid the triumphs of the biochemist? For those who like to deal in things that can be measured, and will accept nothing that cannot be felt with the forefinger, seen with the eye or heard through the bell of a stethoscope, music is still in the hands of the snakecharmer. To such stalwarts music is the moody stuff that women excel in and young couples dance to. It has no place in the quiver of the average therapist. Indeed, it would appear to have become gradually outmoded since medicine left the priesthood and entered the factual edifice of science. While the gods made instruments to plague us and the Evil Eye cast its fascination and malign spirits invaded our distempered bodies, music was often invoked as a charm, carrying the weight of suggestion to those whose malady was largely psychosomatic. But the gradual spread of public dissection, the elementary knowledge of the circulation of the blood, the establishment of medical teaching, the study of dead tissues and the new science of bacteriology served in time to overcome and banish the idea of evil spirits and finally laid the foundation of a new medical science where the art of music found no place. Very soon the microbe replaced the malediction and the virus succeeded the wrath of God. The protozoon was isolated and the vitamin identified. Ingenuity based on observation took the place of imagination guided by superstition; and men countered the ills of the flesh with a more effective armour. The planets had long ceased to prevail; and with the microscope to demonstrate and the test-tube to confirm, the body yielded up many of its secrets. And now there is no tune for the tapping of a hydrocele, no melody for the moulding of a splint. The appendix is extirpated without chamber music and the fever quelled without a flute.

Medicine's proud shield has no music in its quarterings; and yet it finds a diminutive place in the long-neglected study of the disordered mind. Like a secret rediscovered, music came to the mental hospital to arouse the lethargy of some and stem the aimless activities of others. It came at first haphazardly as a mere diversion introduced by some charitable medical officer who was probably appalled by the vacant stare, the noisy inanities and the perseverant activities of the insane. It was but a fleeting item in the entombed routine of the day; but for some it lent a moment's grace to the greyness of a cohibitive existence. Some hospitals, it is reported, now train their own orchestra which plays throughout the patients' meal times, when a decorous atmosphere supersedes an unruly hubbub of clatter and indifferent declamation. For rhythm is infectious. It creeps into some crazy heads and soon has them wagging to a tune, or it slides into certain indifferent feet until they gently tap the floor with melodic beat. Popular tunes may touch the engrams of childhood and the associations of adolescence. Old memories are revived and relived in the mind as they were before sanity's shield was broken. The notes of gaiety knock at the leaden heart—and not always in vain; and the resolutions of a simple harmony may lift the mood for the nonce from the clutch of despair. Music helps to people the solitude of the schizophrenic, and warm the frozen currents in the soul of the melancholic.

Few, indeed, are indifferent to the call of music; but no one will claim that it cures the gross disorders of the mind, or that mental patients having been subjected to the magic of music come clear-headed out of the fog of an established psychosis. No one will suggest that the paretic can be coaxed from his grandeur or the paraphrenic from his delusive world by the strains of music, however near to heaven its harmonies may soar. For though it may calm the savage wolf and make the lion drop his crested mane, it cannot restore sanity to the dement or plant wisdom in the mind of the defective. No one need imagine that the curative effect of convulsion therapy could be supplanted by a roll of drums or a fanfare of trumpets. But anyone conversant with the effect of music upon mental patients will admit the general benefit that it engenders among the depressed and unruly—particularly when one sees the catatonic, indifferent to every plea and insensitive to every command, begin slowly to nod his head to the intangible measure of a tune—the stuporose melancholic take notice of a plaintive melody—or the hard-driven maniac cease his antics for a while when music puts a damper on his tongue and a bridle on his movements. Music does not cure, but it has the power, in many cases, to open the hidden gate so that the troops of a more specific therapy may enter the beleaguered citadel of the mind.

Both music and patients must be selected. It is idle to imagine that a loud-speaker in the ward connected to a master receiving set in the hospital office can stimulate the patients' interests when the programme may vary from a sporting commentary to a compered quiz. Some musical knowledge and appreciation on the part of the person directing the session is essential. A good radiogram and an adequate supply of records far exceed the average broadcast programme. Even a piano in the hands of a moderately gifted performer with a good memory or the capacity to improvise is not to be disdained; and useful changes may be rung by the occasional addition of a violinist, a vocalist or a flautist. Small groups of patients are not only easier to work with, but they seem to gain more than the large and unselected assemblies. Where conditions permit, patients may be introduced to music individually, by beginning with the simplest nursery tunes and continuing with music likely to have been heard in childhood and adolescence; thus the kinæsthetic sense is first stimulated by the rhythm, childish associations are awakened and finally the interest is captured by the integrative effect of more complicated melodies, and a tentative contact with reality may at least be possible. If and when this occurs, music may rest on its laurels while psychotherapy takes charge and sets out to augment the achievement of music by developing fresh interests and buttressing the relinquished powers of adaptation to reality's demands.

The suggested transformation just outlined is more complicated and more fraught with disappointment than it may appear, and may not always reach the desired conclusion; for there are hurdles that cannot be vaulted and rough places that cannot be crossed by many of those who seek the way back to reality and ordered living. Music is a means of captivating the attention. Shakespeare realized this when he said that it had "holped madmen in their wits". It brings a mead of happiness to the dispirited. It relieves emotional tension, and unconscious memories may be abreacted through the medium of association. But its action is still uncertain, and its full potentialities remain untested. Though it may deliver its magic notes to the thalamus, no sentient echo may reach the corridors of the cortex; and the patient, having evinced a furtive pleasure in the music played to him, may glimpse reality with a startled apprehension and quietly turn back to his dream-lit world of

fantasy. Nevertheless Bedlam is a better place with the introduction of music, though Mad Meg and Crazy Tom are still awaiting a melody for their madness.

Beyond the mental hospital, music is scarcely known in the other pavilions of healing, and in the clinics of general medicine it is unheard of by those who still run helter-skelter after the synthetic chemist, counting on the promise of a palliative. But psychosomatic disorders continue to multiply and to persist despite the resources of the pharmacy. Music's day is therefore yet to come. A new science of psycho-acoustics is about to be born; and it may soon open another world to the therapist. At present it is scarcely more than a therapeutic toy in certain of the more progressive mental hospitals and clinics where the simpler experiments are being conducted; but the first portents have recently appeared, and wise men are looking for the star to lead them.

Even now we know that musical therapy has greatly alleviated anxiety states, assisted early schizophrenics and opened a new door for depressives. Folk music and traditional melodies—tunes that have sung themselves through succeeding generations—often have a deeper thrust than persuasive words or logical arguments. But this is not the place to detail the *do-re-mi* of musical therapy, to discuss the relative value of harmony, melody and rhythm or to endeavour to assess the potential value of individual musical compositions in relation to the various psychotic states. Nor can we, at this stage, say a great deal about the type of music best suited to the neurotic. Let it suffice, however, to point out that in this last instance participation in the singing of choral works is of especial value. Apart from this, and speaking in general, the virtue of music as an adjuvant to other forms of treatment has found encouraging proof in the amelioration of stammer, tic and tremor. It implements suggestive therapy; it finds a place in the reeducation of faulty neuro-muscular patterns; it alters muscle tonus and increases the imagination and the interests.

The rise and progress of modern medicine have been dazzlingly spectacular. The microbe has succumbed to the mould. The louse, the mosquito and the rat have ceased to plague us. Victory over the virus is now in sight. Infant mortality has declined; and man has added a new span to his days, though he lives in a doubtful security and in the mounting tension of national antagonisms. He has mastered the secrets of mechanization, and earth's abundance lies at his feet; but his days have become hard-featured, standardized and matter-of-fact. He has lost the serenity of times past. His craze for speed and his inordinate greed have brought a spiritual sickness upon him. He lives in the soul's drouth.

Music will not heal the ills of the flesh. But the day may not be far distant when its boon goes beyond the mental hospital to the wider world of mental strife and emotional tension where, in a way unknown at present, it will lay its blessing upon the spirit.

REG. S. ELLERY,
Melbourne.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

THE INFIRMARY.

[From *The Sydney Morning Herald*, August 19, 1846.][1]

WE are glad to learn that the Bakers Operative Society have subscribed five pounds to the funds of the Infirmary which has been paid to Mr. Thomas Woolley, Treasurer. This subscription entitles them to send three patients to the Infirmary and thirty patients to the Dispensary yearly on the recommendation of their chairman Mr. Robert Gillespie. The three patients may be in the Infirmary at one time or separately: and the privilege must be of much benefit to members of the Society subject to accidents, fevers, inflammations etc. from the nature of their business. The same subscription will also entitle the Society through Mr. Gillespie or the chairman for the time being to three votes at elections of directors and office bearers. It should be more generally known that any person or society, by its chairman or any trustee named first in any will or deed subscribing ten pounds yearly, may have one patient constantly in the Infirmary: that is, may have one bed always occupied, and every attention which skill and charity can bestow paid to the afflicted patient who may occupy it. We are glad to have this opportunity of making these points known to our readers and shall be happy to learn that other societies of tradesmen in town follow the very laudable example set by the Operative Bakers Society. We believe that the rules of the Benevolent Asylum admit of similar privileges which might be embraced without disturbing the duties of surgeons paid to attend sick members and their families at their own houses.

[1] From the original in the Mitchell Library, Sydney.

Medical Societies.

THE MEDICAL SCIENCES CLUB OF SOUTH AUSTRALIA.

A MEETING of the Medical Sciences Club of South Australia was held at the New Medical School, Frome Road, Adelaide, on March 4, 1955.

The Cytochemical Study of Enzymes.

DR. R. A. BARTER presented a brief survey of techniques for the cytochemical study of enzymes. He said that Ehrlich in 1885 had demonstrated the presence of cytochrome oxidase *in vivo* by performing the Nadi reaction. In 1900 Brandenburg introduced a technique for demonstrating leucocyte granules (peroxidase reaction). Robison (1923) showed a high alkaline phophatase activity histochemically in the zone of provisional calcification of bones in rhachitic rats. Gomori (1939) and Takamatsu (1939) independently published an improved method for determining alkaline phosphatase activity by incubating fixed sections in a buffered solution containing glycerophosphate and calcium ions. The precipitate of calcium phosphate was visualized by conversion to black cobalt sulphide. In 1944 Menten, Junge and Green showed a similar localization of alkaline phosphatase by precipitating the alcoholic end of the ester with diazonium salts. Nuclei which were positive with the Gomori-Takamatsu technique failed to show the presence of enzyme when the alcoholic end was precipitated by diazonium compounds. Critical studies of the possibility of diffusion of enzyme or products of substrate splitting (causing false localization in nuclei *et cetera*) were published by Danielli (1946), Martin and Jacoby (1949) and others.

Histochemical techniques had been developed for several other enzymes; acid phosphatase (Gomori, 1941), esterases (Nachlas and Seligman, 1949; Holt, 1952) and succinic dehydrogenase (Seligman and Rutenburg, 1951) were considered as examples of some, and more recent developments for their improvement were outlined. Further critical studies of such techniques were still wanting.

The results of applying the Gomori-Takamatsu procedure with different times of incubation for kidney and duodenum sections prepared by freeze-drying showed that nuclear staining occurred only on prolonged incubation and that sites of high enzyme activity (brush borders) appeared to become negative. The latter observation had been shown by Ruyter (1952) and Danielli (1952) to be due to an alteration in the form of calcium phosphate (non-reactivity for conversion to cobalt sulphide) and not to any gross diffusion from the site of formed calcium phosphate.

By superimposing active sections on sections previously inactivated by various means, a faint staining of nuclei, for example, in the underlying section near to the active section occurred on prolonged incubation. Those observations definitely indicated that enzyme or phosphate ions diffused to the inactivated section and that some degree of artifact must occur with the Gomori-Takamatsu technique. Danielli (1946) showed that sites of affinity for calcium phosphate in inactivated sections (by oxidation of glycerophosphate with hydrogen peroxide) were also the sites of enzyme activity under the usual conditions of the technique.

Dr. Barter went on to say that in collaboration with Professor J. F. Danielli and Dr. H. G. Davies, quantitative studies had been made of the amount of calcium phosphate precipitated at sites in cells; a Cooke, Troughton and Simms interferometer microscope was used. Those studies showed

that reproducible results could be obtained at the same site in a cell several times.

Formed calcium phosphate was dissolved out of the section at a pH of 7·0, and incubation with a solution containing sodium B glycerophosphate and calcium and magnesium ions at a pH of 9·3 was performed again. By that means it was possible to vary the concentrations of substances in the incubating medium and so to study the rate of precipitation of calcium phosphate under different conditions of pH *et cetera*. The concentrations recommended originally appeared to be optimal, but by varying the concentration of calcium ions a means was found for assessing escape of phosphate ions liberated.

Complementary studies on bulk sections of fixed tissue in the test tube confirmed the interferometric observations that a constant amount of enzyme remained at a site in a cell; and also showed that there was an initial diffusion of about 5% of the enzyme when the section was first brought to water. Similar methods showed that less than 5% of phosphate ions liberated escaped into the medium under the usual conditions of concentration of substances in the medium. With those reservations, the interferometric technique offered a reliable approach to quantitative studies of other enzymes as well as alkaline phosphatase at sites in cells.

No conclusive evidence for or against the presence of alkaline phosphatase in nuclei had yet been advanced. A suggested method of microdissecting frozen-dried cells in non-polar liquids for subsequent study of isolated nuclei was outlined.

MEDICAL DEFENCE SOCIETY OF QUEENSLAND.

ANNUAL MEETING.

THE fifty-third annual meeting of the Medical Defence Society of Queensland was held at British Medical Association House, Wickham Terrace, Brisbane, on Wednesday, March 23, 1955, at 5 p.m., the President, DR. NEVILLE G. SUTTON, in the chair.

Annual Report.

The annual report for the year ended December 31, 1954, was adopted. The report is as follows.

The Council of the Medical Defence Society of Queensland has much pleasure in presenting the annual report for the year ended December 31, 1954.

Membership.

The Society has now a membership of 698 as against 659 last year. During the year 63 new members were elected and seven returned to membership. Our losses were due to the following reasons: 25 members left the State, three resigned and three died.

Obituary.

It is with much regret that we record the deaths of the following members: Dr. Alex. H. Marks, who was President for many years and a life member of the Society, Dr. Alan G. Pitt, Dr. T. M. S. Hall.

Office-Bearers and Council, 1954.

The following office-bearers were unanimously reelected by the Council: President, Dr. Neville G. Sutton; Vice-President, Dr. G. W. Macartney; Honorary Treasurer, Dr. T. V. Stubbs Brown; Honorary Secretary, Dr. R. G. Quinn; councillors for the year 1954, Dr. T. R. Biggs, Dr. H. W. Horn, Dr. F. W. R. Lukin, Dr. Athol Quayle, Dr. W. J. Saxton, Dr. F. Garrett Scoles, Dr. J. G. Wagner.

The following councillors, who retired in rotation in accordance with the by-laws, were unanimously reelected: Dr. H. W. Horn, Dr. T. V. Stubbs Brown, Dr. F. W. R. Lukin. Dr. W. J. Saxton, who had been nominated to fill a vacancy on the Council, was unanimously elected.

Medico-Legal.

Two of the cases referred to in last year's report have resulted as follows. One case has been settled out of court, and the other resulted in a withdrawal by both parties after having completed an indenture releasing one another from all claims.

Nine other matters were submitted to the Society during the year, seven of which have been referred to the Society's solicitors for necessary action. The other two were dealt with by the Council, and advice was given to the members.

Finance.

It will be shown by the balance sheet that the net surplus for the year ended December 31, 1954, amounted to £338 19s. 3d.

Some items of income and expenditure are as follows:

	£	s.	d.
Receipts:			
Annual subscriptions, Medical Defence Society of Queensland	361	5	0
Entrance fees	66	3	0
Subscriptions, Indemnity Insurance, Medical Protection Society, Limited, London	3,867	5	9
Interest:			
Commonwealth Government Treasury Bonds and Inscribed Stock	266	7	7
Commonwealth Savings Bank	10	2	6
Expenditure:			
Amount remitted to Medical Protection Society	3,679	0	0
Secretarial and clerical assistance	256	0	0
Rent, postages, duty stamps, bank charges, printing and stationery *et cetera*	33	19	6
Accountancy and audit fee	17	17	0
Legal expenses	55	13	0
Federal income tax for year ended December 31, 1953	24	17	0

The total assets of the Society amount to £9746 4s. 8d.

An amount of £8663 18s. is invested in Commonwealth Inscribed Stock and Bonds.

The current assets include bank balances amounting to £1054 9s. 4d.

NEVILLE G. SUTTON,
President.

Balance Sheet and Financial Statement.

The balance sheet and financial statement for the year ended December 31, 1954, were adopted.

Election of Councillors.

The following councillors, who had retired in conformity with the by-laws of the Society, were unanimously reelected: Dr. G. W. Macartney, Dr. J. G. Wagner, Dr. R. G. Quinn.

Election of Auditors.

Messrs. R. G. Groom and Company, Chartered Accountants (Australia), were reelected auditors for the ensuing year.

Correspondence.

YOUNG DOCTORS AND SPECIALIZATION.

SIR: In answer to what is in the best interests of our profession—should the recent graduate proceed straight forth to his chosen speciality or should he have a background of training in general practice?—granted much may be said on both sides. After thirty years of general practice in country and city with an endeavour to keep abreast of the times by travel, association with members of all specialities, Branch clinical evenings and journals, my summation of the more recent products of our profession is that we are producing more and more highly skilled technicians and less and less good doctors.

As has been said, "human beings are human beings", and they will not be pushed around by garage or jet mechanics. I venture to suggest that many are becoming alive and very wide awake to this fact. I may not be able to interpret correctly the latest biochemical and X-ray findings, but I am still able to diagnose a ruptured ectopic in a back bedroom at 2 a.m., and pacify a distressed householder late at night, this after the day's work from the newborn to senility and all that goes between.

In addition I have learnt to know something of the frailties of human emotions, to know when a little sympathy and kindness is worth many pills and potions; just as on occasions tact and firmness is required. With a sound clinical training and a knowledge of people it is surprising how little outside aid is required. When it is necessary, direct it in the correct channel and forget your vanities.

The success of all branches of our calling is to know our limitations. It is not for me to suggest that every would-be specialist must do a period of general practice, but suffice it to say that if he has done a period of general practice, say for five years, then he is going to become a much better specialist and doctor.

Whilst on the subject of specialists, might I suggest that some of the more recent return to the courtesies and ethics of more mature graduates, in that there is a growing tendency on the part of many that when a patient is referred for an opinion, the next you know he or she is in this or that hospital and that they have done a Cook's tour of other specialists? This is often learnt from friends or relatives or maybe a belated letter from the consultant or a telephone communication from a secretary. Let me have one final say in relation to these female secretaries. The majority are fortunately most pleasant and cooperative, but some are downright rude. Then, too, how often does a secretary 'phone you and politely state that this or that has been arranged, time, place *et cetera*, for you to take it or leave it? I know only too well the difficulty *re* hospital beds and operating theatre times; but at least I expect, after reference of a patient, be it medical or surgical, that the consultant have the courtesy to communicate with me direct and not to leave it to his secretary, who on occasions knows far too much in relation to the patient and at times has added her opinion of the personality of the individual.

Maybe I have been unfortunate with some of these experiences. The sum total of these incidents causes me to reflect that I am outdated in this rapidly changing and commercial age. Nevertheless, I still hold the opinion that the consultant (specialist) should at least set high standards of ethics and cooperate personally with his fellow "G.P.". I am unaware if the various colleges have their own standard of ethics. If they have, then some of their members should be told in plain language for what those ethics stand.

To add this all up, I am still old-fashioned enough to believe that a groundwork in general practice with all its trials, difficulties and knowledge of people, not only in consulting rooms but in their own homes, will make for a better understanding of both sick and well, and a better specialist, who will be able to overcome so often a fragmentary approach to his patients.

The late Sir Thomas Anderson-Stuart advised me when a student: "Never divide the human body into a lot of little compartments and do not separate the mind from the rest, but think in terms of the whole of your anatomy and physiology."

If true thirty years ago, then equally true today, for both specialist and general practitioner.

Yours, etc.,

P. L. K. ADDISON.

241 Oxford Street,
Bondi Junction,
New South Wales.
April 19, 1955.

PYRIMETHAMINE IN EMERGENCY CASES OF MALARIA.

SIR: I have read Dr. W. E. Giblin's paper on "'Daraprim' in the Whagi Valley of New Guinea" (January 2, 1954, page 2) with great interest. As the ideal antimalarial drug is still lacking, it is agreed that every effort should be made to test new additions to our arsenal of chemotherapeutics.

It would appear that Dr. Giblin has, however, aimed too high; he has written: "The objective has been not only to control the overt attack, but *to prevent relapses or reinfection*" (italics by me). It is well known that (*a*) pyrimethamine ("Daraprim") does not prevent relapses any more than quinine, proguanil, mepacrine, chloroquine *et cetera*, and (*b*) there is no known drug which can prevent reinfection.

This, however, is not the main point which induces me to protest, though belatedly (the paper in question did not come to my attention sooner), against the clinical experiments described by the author. He is to be congratulated on his success in so many (partly immune) autochthonous patients. The question arises whether it is ethically justified to experiment on a non-immune, dangerously ill patient who, according to the author, was cold, collapsed, mentally deranged and disorientated, with 13% of infected erythrocytes, and who died "eight hours after his admission, in spite of 75 milligrammes of 'Daraprim'". This certainly was an emergency case in which the oral administration of any drug (either quinine or one of the synthetics) was futile. This fact is confirmed in any text-book on tropical medicine (see, for example, "Manson's Tropical Diseases", thirteenth edition, 1950, page 105: "No time should be lost in injecting quinine dihydrochloride intravenously.") The general expert opinion is that in such cases the slow intravenous injection of eight to ten grains of quinine may save the patient's life.

The Expert Committee on Malaria of the World Health Organization recently wrote in their fifth report (Geneva, July, 1954, Technical Report Series No. 80) ". . . that it is advisable to reserve . . . pyrimethamine for prophylactic purposes", as ". . . its action is not sufficiently rapid to warrant its use in the treatment of acute malaria, at any rate in non-immune subjects . . .". *A fortiori*, pyrimethamine is unsuitable for the treatment of emergency cases.

I think that an emphatic warning against the use of a drug like pyrimethamine in emergency cases is justified.

Yours, etc.,

CH. W. F. WINCKEL, M.D.,
Fellow, The Institute of Tropical Hygiene and Geographical Pathology.

Amsterdam,
Holland,
April 14, 1955.

MORTGAGING THE FUTURE.

SIR: In our letter under the above heading (THE MEDICAL JOURNAL OF AUSTRALIA, February 26, 1955) it was stated that an advertisement for a Director of Anæsthesia at a salary of £2000 *per annum* had been made by the Royal Alexandra Hospital for Children. This was incorrect; the salary offered having been £2500 *per annum*. Our apologies for this unintentional misstatement have been accepted by the hospital, and we should be grateful if you would also publish this correction.

Yours, etc.,

ROBERT B. SPEIRS,
Vice-Chairman, N.S.W. Section, Australian Society of Anæsthetists.

143 Macquarie Street,
Sydney,
April 25, 1955.

THE USE OF PAS IN RHEUMATOID ARTHRITIS.

SIR: It is high time that Dr. Brian G. Haynes (THE MEDICAL JOURNAL OF AUSTRALIA, March 19, 1955) and others ceased to make extravagant claims for the therapeutic efficiency of any single drug in the treatment of a disease with so many variants as rheumatoid arthritis.

In addition to PAS Dr. Haynes admits to prescribing gold, sulphadiazine and rest, and, being a well-qualified and experienced physician, he would naturally attend to psychological adjustments, correct anæmic states, give intra-articular hydrocortone when indicated, apply supports where joints require it, and the many other necessities for improved general health and rehabilitation that individual cases may require. Out of this formidable list he chooses PAS as the master drug. Why not gold? or the sulpha drug? two agents of widely accepted therapeutic value in suitable cases of rheumatoid arthritis.

Following the article by Brous in 1952, PAS, which was then an unrestricted free drug, was given a correspondingly free trial. Reports from my colleagues were unanimous that PAS had very limited value in the treatment of rheumatoid arthritis, which agreed with my own findings.

In addition to PAS and another salicylate, namely, aspirin, extraordinary results have also been claimed for such diverse substances as several of the hormones and intravenous colloidal iodine. "Butazolidin" has been claimed as a cure for most forms of chronic arthritis, and an intravenous iron preparation held to have definite antirheumatic activity.

There is a harmful aspect to such assertions. Since the introduction of cortisone brought rheumatoid arthritis from comparative obscurity to headline news in the lay Press, references to articles in medical journals have frequently been made with embellishments, in syndicated columns. The rheumatoid population have been led to expect some wonder cure, only to be followed by disillusionment and an emotional setback which so often leads to joint deterioration.

Yours, etc.,

149 Wickham Terrace, Brisbane,
April 18, 1955.

JOHN SHANASY.

JAMES THOMAS RUDALL, F.R.C.S. (1828-1907): LIFE AND JOURNAL FOR THE YEAR 1858.

SIR: Would you allow me to thank Bryan Gandevia for his kind reference (M. J. AUSTRALIA, April 16, 1955) to my observations upon the splendid old Victorian practitioner (*Tr. Ophth. Soc. Australia*, 1947)? Also, I wish to congratulate him on his paper (M. J. AUSTRALIA, December 25, 1954).

It appears that when I wrote my paper few Victorians had heard of Rudall, although his son, James Ferdinand Rudall, was well remembered as a surgeon to the Victorian Eye and Ear Hospital. I have a suspicion that the son was named Ferdinand after the incredible Baron Sir Ferdinand von Mueller (as he was often addressed), K.C.M.G., F.R.S., who was *persona grata* in medical circles in the latter half of last century.

Probably the last surviving practitioner who knew Rudall was the revered Edward Leslie Gault, whose obituary appreciation by Leonard Mitchell sadly appears in the issue first mentioned above.

I think that I can justly claim that James Thomas Rudall was "the father of ophthalmology in Australasia".

Yours, etc.,

207 Walker Street,
North Sydney,
April 20, 1955.

DARCY WILLIAMS.

Obituary.

DENIS ADRIAN PRITCHARD.

WE are indebted to Surgeon Rear-Admiral L. Lockwood for the following appreciation of the late Surgeon Rear-Admiral D. A. Pritchard.

Denis Adrian Pritchard was born on April 26, 1895, in Sydney. He was educated at Sydney Grammar School and the University of Sydney, graduating in the faculty of science in 1914. During World War I he worked in England in munitions. Returning to Australia, he embarked on a medical course and took his bachelor's degrees in medicine and surgery at the University of Sydney in 1922. On August 3, 1923, he joined the Royal Australian Navy as a surgeon lieutenant. During 1929, he gained a diploma in tropical medicine at the University of Sydney and also received promotion to the rank of lieutenant-commander. He proceeded to London in 1934 for his promotion course to surgeon commander at the London Hospital and Royal Naval College, Greenwich. As a result of the examination, he gained one year's accelerated time, and his seniority as surgeon commander was antedated to 1934. He became a member of the Royal College of Physicians of London in 1935 and returned to Australia in the following year. In 1937 he was elected a Fellow of The Royal Australasian College of Physicians. During the years from 1923 to 1937 he had served in a number of Royal Australian Navy ships and establishments, including His Majesty's Australian Ships *Platypus, Anzac, Melbourne, Moresby, Sydney* and *Canberra*, and shore establishments in Sydney and at the Royal Australian Navy College, Jervis Bay. On the outbreak of World War II he was serving in H.M.A.S. *Canberra*, but transferred to H.M.A.S. *Perth* in June, 1940. Owing to an injury he joined H.M.A.S. *Leeuwin* in November, 1940, and then served in H.M.A.S. *Penguin* until April, 1942. At that time he transferred to H.M.A.S. *Australia* and subsequently took part in the Coral Sea battle and in landings at Guadalcanal and served in the New Guinea and Philippines areas. He remained in H.M.A.S. *Australia* until July, 1944. After a further period of shore service he was appointed Director of Naval Medical Services on January 30, 1946, with the rank of surgeon captain, in succession to Surgeon Rear-Admiral W. J. Carr, C.B.E., and held the appointment until his death on March 11, 1955.

During his term as Director of Naval Medical Services, Admiral Pritchard held the appointments of Honorary Physician to His Royal Highness the Duke of Gloucester, while he was Governor-General of Australia, Honorary Physician to His late Majesty King George VI from 1946 to 1951 and Honorary Physician to Her Majesty Elizabeth II from February, 1952, until his death. For his services he was made a Commander of the Most Excellent Order of the British Empire in the New Year honours of 1952.

The above record reveals that Admiral Pritchard served his country in the Royal Australian Navy with great distinction over a period of nearly thirty-two years. He was always a keen student, of vigorous and inquiring outlook, and his early scientific training was expressed in his interests. It was often remarked that he had a highly scientific mind. In his professional work, his main leaning was towards medicine, but his outside interests were many. He had a great love of gardening, being a noted cultivator of prize camellias, in which he took much pride, and a member of the American Camellia Society. Another of his interests was craft work, testimony towards which was his skill in making the most exquisite lampshades. He was also an avid reader of scientific publications.

It is sad that Admiral Pritchard did not live to enjoy his retirement, as he died just a few weeks before this was due. His task as Director of Naval Medical Services was no easy one after World War II, and there is no doubt that the heavy responsibility and great worry occasioned by his duties took heavy toll of his constitution. Our sympathy goes to his wife and daughter, who have the comfort that their husband and father gave all his ability and loyalty in the service of his country. Admiral Pritchard's funeral at Christ Church, South Yarra, and Springvale Crematorium was memorable. Her Majesty the Queen commanded that her personal representative be present. A very largely attended ceremony with all naval honours showed fitting respect to a distinguished officer.

Dr. C. R. Furner writes: The death of Surgeon Rear-Admiral D. A. Pritchard removes a fine and, as befitted his service, rather silent member of the medical profession who was widely respected and loved by his friends.

Denis Pritchard was born in Sydney and educated at Hayfield Preparatory School and Sydney Grammar School. A great admirer of the late Sir Edgeworth David, he was influenced by him to undertake a science course at the University of Sydney with a special interest in geology. Then came the first World War, and, having been rejected for active service, Pritchard spent some time munition-making. Towards the end of the war he decided to do medicine, in which he graduated in 1923. Strangely enough, he did not get a hospital appointment and entered the Navy as a medical officer, soon afterwards gaining his diploma in tropical medicine. In 1934, now a lieutenant-commander, he was sent to London to a naval medical officers' course in all branches of medical work. Officers from the Royal Navy and all parts of the Empire—as it was then—attended. At the end of the course was an examination for promotion to commander. Pritchard received the highest marks by a big margin and would have won the Gilbert Blane Medal had this not been restricted to officers of the Royal Navy. However, as compensation, he was granted a further three months' leave to study and sit for the membership examination of the Royal College of Physicians (London), which he passed on his first attempt. He was later elected a Foundation Fellow of The Royal Australasian College of Physicians (the meetings of which he almost invariably attended). In the second World War he was in the *Canberra, Perth* and *Australia*. In 1946, now a surgeon captain, he became Director of Naval Medical Services and Honorary Physician to the King. Later he became Honorary Physician to Her Majesty the Queen, rising to surgeon rear-admiral two years ago, being the first serving officer to attain this rank in the Royal Australian Navy. The absence of Press publicity of the Naval Medical Service is evidence of the efficiency of Pritchard's administration.

His death came rather unexpectedly, though he had been far from well for several years. He had been looking forward to retirement in April of this year at the age of sixty, and planned after nine years in Melbourne to return to his home and garden at Wahroonga, which he loved, there to grow flowers and make furniture and enjoy the hobbies which meant so much to him. He was particularly interested in camellias, on which he was an authority. He could do beautiful cabinet-making and upholstery. He loved classical

music and the ballet and reading. At one time photography was a hobby, especially of children, in whom he was very interested. With all these interests it is no wonder that his social life was rather limited to those with similar tastes.

Denis Pritchard was truly a cultured and a good man, with broad sympathies and wide interests. His sense of justice and ability provided the factors for his success in his work, whilst his devotion to his wife and daughter and his loyalty to his friends caused him to be loved and now sadly missed by his family and those who knew him well. To his wife (a daughter of the late Reverend Canon Portus) and daughter the deepest sympathy of many will be extended.

FRANCIS JOHN MEAGHER.

DR. TREVOR TELFER has sent the following appreciation of the late Dr. Francis John Meagher.

It was with infinite sorrow that I learned of the death of John Meagher on January 26, 1955, in Melbourne, at the age of thirty-one years. I am one of many who had the great privilege of being closely associated with him during his student days at the University of Melbourne from 1942 to 1948, and in the succeeding years following graduation.

As a student, during the time that he was at Trinity College, and at the Alfred Hospital clinical school, his subsequently manifest scholastic ability was perhaps somewhat overshadowed by his sporting prowess, in particular in athletics and football, and by his always enviable zest for a fuller life than that commensurate with pure scholastic achievement. He achieved life, and he graduated M.B., B.S. in October, 1948.

As a resident medical officer at the Launceston General Hospital and the Royal Hobart Hospital in 1949 and 1950, his delightful enthusiasm, diligence and sound clinical judgement were readily appreciated by the staff and by his patients, and his gaiety and outstanding personal charm immeasurably enriched the lives of those of us who were his colleagues at this time.

In England in 1952 and 1953 he held several hospital appointments in medicine, including a period at the Post-graduate Medical School of London, and became a member of the Royal College of Physicians in 1953.

He had an insatiable love of travel and an equally great interest in the lives of the people of the various countries he visited. A lasting impression, gained during summer holidays spent with him in Europe, is of this tall, youthful, fair-haired figure, apparently inextricably seated at the wheel of a tiny 1931 Austin, which he lovingly nursed across many of the higher mountain passes of France, Switzerland and Italy, and along rocky coastal roads in Spain, leaving behind him countless people who, though never having known his name and having met him for merely a few minutes, will long remember him as a friend.

He returned to Australia in December, 1953, and had recently been appointed an honorary out-patient physician to the Alfred Hospital, Melbourne.

With his untimely death the world has lost a remarkable man, one who, more than any I have known, had all the grace and adventure of youth, its laughter, its wisdom and its wonder. The medical profession has lost a young physician of outstanding quality, of unceasing curiosity and balanced judgement, and of potential greatness. And we who were his friends will not find a more charming or exhilarating colleague, or a finer friendship.

JOHN HARDIE.

DR. E. S. MEYERS has sent the following appreciation of the late Dr. John Hardie.

Dr. John Hardie was a son of the late Sir David Hardie, and his passing severs a long continuity of service to the public.

I first knew him when we were at school together and subsequently at the University of Sydney. In 1915, when I joined the resident medical staff of the Brisbane Hospital, Dr. John Hardie was the medical superintendent and had to assist him a staff of five medical officers. The hospital was then run by a committee with Miss Grace Wilson as matron. (Miss Wilson afterwards became Principal Matron of the first Australian Imperial Force.) Some months later Dr. Hardie left for active service, and I did not see him again until 1918, the occasion being a mass gas attack on the Eleventh Brigade with some 800 casualties, Dr. Hardie being at that time regimental medical officer of the Forty-Second Battalion.

On his return from the war he served for many years as honorary surgeon to the Brisbane Hospital and carried on a private practice that his father had established. Many of his old patients whom I have met have spoken to me of Dr. Hardie's kindness and consideration.

In the second World War he was engaged extensively on medical boards, and with Dr. Ewing Thomson must have examined countless hundreds of the second Australian Imperial Force.

Dr. Hardie's passing reduces the resident medical staff of 1915 from six to three.

Naval, Military and Air Force.

APPOINTMENTS.

THE following appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 13, of March 17, 1955.

AUSTRALIAN MILITARY FORCES.

Australian Regular Army.

Royal Australian Army Medical Corps (Medical).

2/40131 Captain H. Gayst is placed upon the Retired List (Eastern Command) with permission to retain his rank and wear the prescribed uniform, 3rd February, 1955.

The Short Service Commission granted to 3/40054 Major (provisionally) J. H. Cater is extended until 25th June, 1956.

1/8062 Honorary Captain J. K. O'Reilly is appointed from the Reserve of Officers, and to be Captain, 10th January, 1955, with a Short Service Commission for a period of one year.

Citizen Military Forces.

Eastern Command.

Royal Australian Army Medical Corps (Medical).—To be Captain (provisionally), 7th February, 1955: 2/217015 Verner William Bow.

Southern Command.

Royal Australian Army Medical Corps (Medical).—To be Captain (provisionally), 4th February, 1955: 3/111532 Howard Alfred Marks.

Central Command.

Royal Australian Army Medical Corps (Medical).—4/31988 Captain R. A. Barter ceases to be seconded for post-graduate studies in the United Kingdom, 26th October, 1954. 4/32062 Honorary Captain H. W. Welch is appointed from the Reserve of Officers, and to be Captain (provisionally), 17th December, 1954.

Reserve Citizen Military Forces.

Royal Australian Army Medical Corps (Medical).

Northern Command.—To be Honorary Captains: John Joseph Breen, Frederick Allan George, and Reginald Sydney Neilsen, 3rd January, 1955, and Bernard Joseph Knapp and Kevin Patrick Kennedy, 31st January, 1955.

Southern Command.—To be Honorary Captains: John David Henry Muir, 1st January, 1955, and Ian Gellatley Lyall, 4th January, 1955.—(Ex. Min. No. 49—Approved 10th March, 1955.)

ROYAL AUSTRALIAN AIR FORCE.

Permanent Air Force.

Medical Branch.

The probationary appointment of Flight Lieutenant C. R. G. Stoddart (015209) is confirmed.

Air Force Reserve.

Medical Branch.

Flight Lieutenant I. H. Ogilvy (257507) is promoted to the temporary rank of Squadron Leader, 2nd February, 1955.

The Royal Australasian College of Physicians.

RESEARCH FUND.

THE Royal Australasian College of Physicians invites applications for grants from the Research Fund of the College. Grants may be made to individuals for research fellowships tenable in Australasia or overseas, or as grants-in-aid to approved institutions or departments to enable a particular research project to be undertaken under approved circumstances. Applications should be made on the prescribed form, which may be obtained from the Honorary Secretary of the College at 145 Macquarie Street, Sydney, and should be lodged with the Honorary Secretary before August 1, 1955.

Medical Prizes.

DAVID ANDERSON-BERRY PRIZE (1956).

A DAVID ANDERSON-BERRY silver-gilt medal, together with a sum of money amounting to about £100, will be awarded in 1956 by the Royal Society of Edinburgh to the person who, in the opinion of the Council, has recently produced the best work on the therapeutical effect of X rays on human diseases. Applications for this prize are invited. They may be based on both published and unpublished work and should be accompanied by copies of relevant papers. Applications must be in the hands of the General Secretary, Royal Society of Edinburgh, 22, 24 George Street, Edinburgh, 2, by March 31, 1956.

Public Health.

DANGEROUS DRUGS ACT, 1934, OF SOUTH AUSTRALIA.

THE following proclamation has been published in *The South Australian Government Gazette*, Number 17, of April 21, 1955.

SOUTH AUSTRALIA, *to wit.* — *Proclamation by His Excellency the Lieutenant-Governor of the State of South Australia.*

(L.S.) J. M. NAPIER.

BY virtue of the provisions of the Dangerous Drugs Act, 1934, and all other enabling powers, I, the said Lieutenant-Governor, with the advice and consent of the Executive Council, do hereby—

1. Declare that subsection (1) of section 6 of the said Act shall cease to apply to—

(1) Dihydrohydroxymorphinone and its salts.

(2) 6-Methyldihydromorphine and its salts.

2. Declare that the said Act shall apply to the drugs specified in the schedule hereto in the same manner as it applies to the drugs mentioned in subsection (1) of section 4 thereof.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED APRIL 16, 1955.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.[2]	Australian Capital Territory.	Australia.[3]
Acute Rheumatism	4(1)	..	6(3)	..	1	..	..	..	11
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	1	..	26	..	..	..	..	..	27
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	1	9(5)	5(4)	..	..	..	..	1	16
Diphtheria	12(7)	12(8)	1	1	7(7)	..	..	..	33
Dysentery (Bacillary)	..	3(3)	7(7)	10	3(1)	2(1)	..	1	26
Encephalitis	..	1	..	..	..	..	..	..	1
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	44(19)	60(32)	..	7(2)	7(3)	2	..	..	120
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	3	..	..	..	..	..	3
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	..	1	1(1)	..	..	..	..	..	2
Ophthalmia	..	..	..	..	14	..	..	..	14
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	13(5)	7(2)	3(1)	1(1)	..	..	..	..	24
Puerperal Fever	2(2)	..	..	..	..	..	..	..	2
Rubella	..	12(7)	1	1	4(1)	..	..	..	18
Salmonella Infection	..	..	..	..	..	..	..	..	..
Scarlet Fever	13(9)	29(15)	2(1)	3(3)	2(1)	1(1)	..	..	50
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	..	..	..	..	..	..
Trachoma	..	..	..	..	..	..	..	..	..
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	28(23)	29(17)	15(8)	4(2)	7(6)	3(1)	..	..	86
Typhoid Fever	..	..	..	..	..	..	..	..	..
Typhus (Flea-, Mite- and Tick-borne)	..	..	2	..	2(2)	..	..	..	4
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

[2] Figures not available.

[3] Figures incomplete owing to absence of returns from Northern Territory.

THE SCHEDULE.

(1) Dihydrohydroxymorphinone and its salts.

(2) 6-Methyldihydromorphine and its salts.

(3) Isopropyl and other esters of 1-methyl-4-phenylpiperidine-4-carboxylic acid and their salts.

(4) 4,4-diphenyl-6-dimethylamino-3-hexanone and its salts.

(5) β-4,4-diphenyl-6-dimethylamino-3-heptanol (betamethadol) and its salts.

(6) 4,4-diphenyl-6-piperidine-3-heptanone and its salts.

(7) Any preparation, admixture, extract, or other substance containing any proportion of any of the substances mentioned in this schedule.

Given under my hand and the public seal of South Australia, at Adelaide, this 21st day of April, 1955.

By command,

D.P.H., 2078/1953. COLIN D. ROWE, for Chief Secretary.

Congresses.

THIRD WORLD CONGRESS OF JEWISH PHYSICIANS.

THE third World Congress of Jewish Physicians will be held in Israel between August 10 and 24, 1955, under the auspices of the Israel Medical Association.

Membership dues are twenty dollars for each participant, but physicians who belong to overseas Fellowships of the Israel Medical Association will pay only fifteen dollars. The tourist agency appointed to look after journeys to Israel for the congress is Mendes Tours and its agents in various countries, but that is not exclusive and individuals are free to choose the agency they prefer. Opportunity will be given to participants to tour Israel, and visit medical and social establishments, and there will be all kinds of official, municipal and organizational receptions.

The Legation of Israel, 84 Pitt Street, Sydney, will be happy to assist with information and advice any Jewish physician who is contemplating attending the congress.

Australian Medical Board Proceedings.

QUEENSLAND.

THE following have been registered, pursuant to the provisions of *The Medical Acts*, 1939-1948, as duly qualified medical practitioners: Georgeson, Laurence Edwin, M.B., B.S., 1954 (Univ. Sydney); Sutherland, Diana May, M.B., B.S., 1953 (Univ. Melbourne).

The following additional qualification has been registered: Mellick, Selim Abraham, F.R.C.S. (England), 1953.

Nominations and Elections.

THE undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

McGarn, Francis Ralph, M.B., B.S., 1953 (Univ. Sydney), 1 Kensington Road, Summer Hill, New South Wales.

The undermentioned has applied for election as a member of the Victorian Branch of the British Medical Association:

Horan, Margaret Burton, M.B., B.S., 1932 (Univ. Adelaide), M.R.C.P. (London), 1936, M.R.A.C.P., 1941, 55 Collins Street, Melbourne.

Medical Appointments.

Dr. T. G. H. Hogg has been appointed President of the Physiotherapists Registration Board of Tasmania.

Dr. A. L. McMillar has been appointed a member of the Physiotherapists Registration Board of Tasmania.

Dr. L. J. Daly has been appointed an honorary medical officer at the Port Pirie Hospital, South Australia.

Dr. D. A. Dowie has been appointed an honorary medical officer at the Port Pirie Hospital, South Australia.

Dr. R. D. Hammill has been appointed medical superintendent (part time) at the Port Pirie Hospital, South Australia.

Deaths.

THE following deaths have been announced:

BROWN.—Donald Montague Brown, on April 24, 1955, at Echuca, Victoria.

SAWERS.—William Campbell Sawers, on April 27, 1955, at Wentworth Falls, New South Wales.

Diary for the Month.

MAY 10.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
MAY 13.—Tasmanian Branch, B.M.A.: Branch Council.
MAY 13.—Queensland Branch, B.M.A.: Council Meeting.
MAY 16.—Victorian Branch, B.M.A.: Finance Subcommittee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all contract practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £5 *per annum* within Australia and the British Commonwealth of Nations, and £6 10s. *per annum* within America and foreign countries, payable in advance.